STATEMENT OF

THE ALABAMA STATE BOARD OF MEDICAL EXAMINERS

On December 12, 2024, the Alabama State Board of Medical Examiners ("the Board") considered a petition submitted by Grady B. Core, M.D., FACS ("Petitioner") requesting that the Board adopt certain rules pursuant to Ala. Code § 41-22-8 and Ala. Admin. Code r. 540-X-1-.09, to regulate and permit physicians to train and delegate certain classes of licensed professionals to inject neuromodulators[1] and dermal fillers for cosmetic purposes.

FACTS PRESENTED

The Board first reviewed this petition at its November 14, 2024, meeting. The Board voted to defer final consideration of the petition to its December 12, 2024, meeting, so that other interested stakeholders could submit their viewpoints. The Board received written responses to the petition from the Alabama Board of Nursing ("ABN"), the Alabama Dermatology Society ("ADS"), the American Academy of Dermatology Association ("AAD"), and the American Society for Dermatologic Surgery Association ("ASDS").

Petitioner presented the following facts and assertions in support of his petition[2]:

> The State of Alabama is the only state in the U.S. where delegated injectors cannot perform cosmetic injections under supervision. This archaic restriction regarding cosmetic injectables has resulted in outside competition taking patients from Alabama providers and preventing Alabama aesthetic providers from competing on a national level, with those from other states. This also has resulted in a lack of convenience for Alabama patients in regards to the availability in other states.
>
> Since there is no data [sic] which supports the practice of cosmetic injectables being administered by non-physician injectors as unsafe, and since there is no data [sic] to demonstrate development of resistance to neuromodulators by multiple provider sites, we feel that the time has come for the board to allow delegated but supervised

[1] The terms "neuromodulator," "botulinum toxin A," and "botox" are hereinafter used interchangeably to refer to the five botulinum toxins that are FDA-approved for cosmetic use.

[2] A complete copy of the petition is attached as Attachment A.

> Level I delegates, as have been approved in the recently passed laser rules, to provide these services to patients of Alabama.
>
> Our goal is to increase supervision and maintain the practice of cosmetic injectables as the practice of medicine in Alabama by mirroring the recently passed laser rules which, will ensure safety for the patient and allow for better access while at the same time allowing providers to provide their services in a more competitive manner as is done in every other state.
>
> Supervision and Safety are the cornerstones of these rules.
>
> Since safety data does [sic] not show nurse injectors have higher complications and there is no valid argument to prevent this practice on a safety basis or a resistance basis, we conclude that the only reason for certain physician groups to advocate for physician only injectables is based only on the premise of a turf war and an attempt to prevent competition. This is not a valid reason to prevent this service from being more available to the citizens of Alabama.

Petitioner further states in the introduction to his "Guidelines for Nurse Injectors" that "the procedures of injecting neuromodulators and dermal fillers – is the practice of medicine in the state of Alabama."

Opposition from the ABN[3]:

The ABN opposes the petition because "the ABN believes the injection of neuromodulators and dermal fillers constitutes the practice of nursing." The ABN stated that they agree with Petitioner that "there is no data [sic] which supports the practice of cosmetic injectables being administered by non-physician injectors as unsafe," but reject the regulatory model proposed by him. Instead, the ABN proposed the following:

> In conclusion, the ABN agrees that registered nurses who have completed an organized program of study, engaged in supervised clinical practice, and demonstrated clinical competence both initially and periodically, may inject neuromodulators/botulinum A and dermal fillers pursuant to an ABN-approved standardized procedures [sic] and an order from a lawful prescriber. ABN also agrees that as lawful prescribers, CRNPs should be able to evaluate patients and order treatment using neuromodulators/botulinum toxin A and dermal fillers, in addition to performing the injections. ABN believes this skill should be included on the standard protocol for CRNPs and CNMs for consideration by the

[3] A complete copy of the response is attached as Attachment B.

> collaborating physician and CRNP/CNM at the time of completing the collaborative practice application. It is neither necessary nor appropriate for ALBME to promulgate rules which purport to prescribe the training requirements for RNs and CRNPs/CNMs. Rules related to collaborative practice for CRNPs and CNMs are initiated in the Joint Committee, and rules related to the scope of practice for RNs are the province of the ABN.

Opposition from the ADS[4]:

ADS opposes the petition, stating: "Our primary concern for patient safety prompts us to adamantly oppose any rule that allows nurse practitioners, nurses, or physician assistants to inject dermal fillers." ADS cited publications for its position that the injection of dermal fillers by persons other than physicians is unsafe to the public, stating:

> Over the past 10 years, an increase in all dermal filler injections and related complications has been well documented in the literature [1-9] [5]. The most serious of these are ischemic complications including tissue necrosis, stroke, blindness, and death [1-9]. As this phenomenon becomes better understood, it has become more important than ever for all injectors to have a detailed knowledge of injection anatomy, years of experience in dermal filler injection, and a keen understanding of the sometimes subtle presentation of an ischemic event. Injectors should possess the correct tools available to manage an emergency situation and a commitment to maintain an education in the latest literature in this rapidly changing landscape [18]. The most important factor in the ultimate outcome of these ischemic complications is the timeframe in which they are diagnosed and treated [16,17,18].
>
> While medical spas and other non-physician offices provide easier access such as shorter wait times, lower prices, and a less rigorous clinical environment [15], these "clients" often become new patients to dermatologists when complications occur and cannot be managed properly by the original injector [11]. In fact, many patients with complications from injection visits never return to the provider that caused them, creating an ongoing perception of safety among inexperienced injectors [Zhou et al]. In addition, the companies that distribute dermal fillers have a vested interest in lowering the bar for entry into this field, lulling potential injectors and patients into a sense of comfort [13] and creating a perception that dermal fillers are safe [11,13]. Unfortunately, these complications have exponentially increased in incidence across the United States as non-physicians have gained the ability to inject. These emergency complications, when

[4] A complete copy of the response is attached as Attachment C.
[5] The cited documents, as well as other supporting documents, are attached as Attachment D.

> unrecognized and mishandled, result in much more morbidity and, in some cases, mortality than is acceptable.

ADS attached approximately 44 documents, including published studies, supporting its position.

Opposition from AAD and ASDS[6]:

AAD and ASDS sent a joint letter to the Board to share "concerns" with the petition. AAD and ASDS claim to jointly represent "more than 17,000 dermatologists nationwide." AAD and ASDS state that "[p]rocedures by any means, devices or instruments that can alter or cause biologic change or damage the skin and subcutaneous tissue constitute the practice of medicine and surgery. This includes the use of foreign or natural substances by injection or insertion." AAD and ASDS stated that the injection of neuromodulators and dermal fillers "should only be performed by a physician or appropriately trained non-physician personnel under the direct, onsite supervision of an appropriately trained physician." However, the petition, in their view, "jeopardize[d] patient safety" by permitting non-physicians who possess "less clinical experience than a physician" to inject neuromodulators and dermal fillers under unsafe conditions and without proper training:

> "Unlike physicians, non-physicians are not required to complete a residency program or demonstrate competency in procedures involving skin and soft tissue augmentation with products that can alter or damage living tissue. It is of upmost importance that the physician or non-physician performing procedures with neurotoxins (such as botulinum toxin) or dermal fillers have specific, long-term training (such as medical residency in dermatology or plastic surgery). The education for non-physicians does not include this type of intense training; additionally, any short-term training program offered by manufacturers of these products does not adequately protect public safety.

AAD and ASDS cited the American Medical Association position statement that "Cosmetic medical procedures, such as botulinum toxin injections, dermal filler injections, and laser and intense pulsed light procedures, be considered the practice of medicine." AAD and ASDS

[6] A complete copy of the response is attached as Attachment E.

concluded by asking the Board to "oppose the request to expand the scope of practice of CRNPs, PAs, and RNs to include the administration of botulinum toxin A and dermal fillers for cosmetic purposes."

THE PETITION

Petitioner requests that the Board adopt a system of rules to govern all aspects of the injection of neuromodulators and dermal fillers by licensed persons other than physicians. Specifically, Petitioner seeks the adoption of rules permitting physicians to train, supervise, and delegate these procedures to assistants to physicians, certified registered nurse practitioners, and registered nurses. Petitioner models his request on Board Rule 540-X-11 Guidelines for the Use of Lasers and Other Modalities Affecting Living Tissue.

ANSWER

The Board considers the decision to order, inject, and administer a neuromodulator, like botulinum toxin A, and dermal fillers, to be the practice of medicine. However, assistants to physicians ("PAs") and certified registered nurse practitioners ("CRNPs") are permitted under state law to engage in certain advanced practices pursuant to a supervisory or collaborative agreement, respectively, with a physician and pursuant to written protocols. The Board finds that Petitioner's request is most appropriately addressed through the issuance of new protocols for PAs and CRNPs. While the Board has the authority to issue protocols for PAs on its own authority, any protocol or rule affecting the practice of CRNPs must first be recommended by the Joint Committee consisting of the Board and ABN. If the Board were to adopt rules as requested by Petitioner, these rules would likely violate the law regulating collaborative practice with CRNPs. Moreover, ABN's objection to these rules necessitates the Board's denial of the petition as it relates to CRNPs. Accordingly, it is the decision of the Board not to adopt the Petitioner's requested rules.

The Board reserves the right to reconsider the substance of Petitioner's request in connection with researching and drafting a specialty protocol for PAs and CRNPs to administer botulinum toxin A by injection under the supervision of or in collaboration with an appropriately trained physician.

DISCUSSION

The "practice of medicine" means "to diagnose, treat, correct, advise, or prescribe for any human disease, ailment, injury, infirmity, deformity, pain, or other condition, physical or mental, real or imaginary, by any means or instrumentality." Ala. Code § 34-24-50(1). Botox Cosmetic, the most well-known version of botulinum toxin A, is an FDA-approved "prescription medicine that is injected into muscles and used to improve the look of moderate to severe frown lines between the eyebrows (glabellar lines) in adults for a short period of time."[7] It can also be injected around the eyes to temporarily improve the look of crow's feet lines in adults.[8] The spread of the toxin after administration can cause trouble breathing, swallowing, and even death.[9] The FDA currently approves five versions of the botulinum toxin for cosmetic use.

A "dermal filler" means the "injection of synthetic substances (e.g., hyaluronic acid, calcium hydroxyapatite, polymethylmethacrylate, Poly-L-lactic acid), collagen, or fat in order to increase the amount of collagen in a body area."[10]

Botulinum toxin and dermal fillers are used to "correct" or "treat" a human "deformity," "injury," "infirmity," or other condition; therefore, the decision to inject or administer any of these instrumentalities is the practice of medicine.

[7] https://www.fda.gov/media/77359/download (Attachment F)
[8] *Id.*
[9] *Id*.
[10] Rhode Island Board of Medicine (Attachment G), pg. 10.

The ABN argues that a registered nurse may, with many caveats and qualifiers, capably inject a neuromodulator following a lawful order and "pursuant to an ABN-approved standardized procedures [sic]."[11] ABN objects to Petitioner's request, stating "[i]t is neither necessary nor appropriate for ALBME to promulgate rules which purport to prescribe the training requirements for RNs." While it is not appropriate for the ABN to presume to create procedures for RNs to perform medical procedures, the inverse does not necessarily hold true. A physician who delegates a task to a non-physician is legally responsible for that person's performance[12], and the physician is responsible for ensuring that the non-physician is adequately trained to perform the task.[13] To do this, the physician must be aware of and have some influence over the training of his or her delegates. Accordingly, the Board cannot agree with ABN's apparent desire to establish training and procedures for skills that constitute the practice of medicine.

The Board also notes the strong objection registered by the ADS, ASDS, and AAD against the injection of dermal fillers by non-physicians. These groups supplied ample evidence to the Board in support of their position that the injection of dermal fillers by non-physicians poses a weighty risk of harm to patients.[14] Both Petitioner and the ABN stated that evidence did not exist to support a risk of harm to patients; however, the evidence supplied by ADS, ASDS, and AAD rebuts this representation. Petitioner's request does not differentiate between neuromodulators and dermal fillers, yet the evidence before the Board supports treating the injection of neuromodulators and dermal fillers as separate skills. This failure of the proposal to appropriately distinguish

[11] Attachment B, page 3.
[12] Board opinion of March 23, 1999 (Attachment H).
[13] *See Frazier v. Gillis*, 85 So. 3d 443, 447 (Ala. Civ. App. 2011).
[14] Attachment D, *passim*.

between neuromodulators and dermal fillers provides an additional basis for declining to adopt the proposal.

Nevertheless, the substance of Petitioner's request to allow certain non-physicians to inject neuromodulators merits additional study by the Board. The method of Petitioner's request – the adoption of rules by the Board concerning the practice of PAs, CRNPs, and RNs – runs against several legal barriers. The most notable of these is the requirement that "[t]he joint committee shall be the state authority designated to recommend rules and regulations to the State Board of Medical Examiners and the Board of Nursing for the purpose of regulating the collaborative practice of physicians and certified registered nurse practitioners and certified nurse midwives." Ala. Code § 34-24-85. Although the Board could conceivably adopt Petitioner's rules in such a way as to be solely applicable to PAs, this would defeat Petitioner's purpose. And such a decision would run against the history of similar actions by the Board. Specifically, the Board has endeavored to utilize practice protocols, rather than rules, to delineate new or additional skills that PAs and CRNPs can practice. Consequently, although the Board must decline to adopt Petitioner's request, the Board may use the information provided by Petitioner, ABN, ADS, ASDS, and AAD as it considers the propriety of adding the injection of neuromodulators for cosmetic purposes to the skills that a PA or CRNP may perform within a collaborative or supervised practice.

This decision is based upon the precise facts presented and upon statutes and rules currently in existence.

DONE this _20th__ day of December, 2024.

C.M.A. "Max" Rogers, IV, M.D.
Chairman
Alabama State Board of Medical Examiners

ATTACHMENT A

CORE PLASTIC SURGERY

Alabama Board of Medical Examiners,

The State of Alabama is the only state in the U.S. where delegated injectors cannot perform cosmetic injections under supervision. This archaic restriction regarding cosmetic injectables has resulted in outside competition taking patients from Alabama providers and preventing Alabama aesthetic providers from competing on a national level, with those from other states. This also has resulted in a lack of convenience for Alabama patients in regards to the availability in other states.

Since there is no data which supports the practice of cosmetic injectables being administered by non-physician injectors as unsafe, and since there is no data to demonstrate development of resistance to neuromodulators by multiple provider sites, we feel that the time has come for the board to allow delegated but supervised Level I delegates, as have been approved in the recently passed laser rules, to provide these services to patients of Alabama.

Our goal is to increase supervision and maintain the practice of cosmetic injectables as the practice of medicine in Alabama by mirroring the recently passed laser rules which, will ensure safety for the patient and allow for better access while at the same time allowing providers to provide their services in a more competitive manner as is done in every other state.

Supervision and Safety are the cornerstones of these rules.

Since safety data does not show nurse injectors have higher complications and there is no valid argument to prevent this practice on a safety basis or a resistance basis, we conclude that the only reason for certain physician groups to advocate for physician only injectables is based only on the premise of a turf war and an attempt to prevent competition. This is not a valid reason to prevent this service from being more available to the citizens of Alabama.

Sincerely,

Grady B. Core, MD, FACS
gradycore@gmail.com
205-520-4458

3595 Grandview Parkway, Suite 150
Birmingham, Alabama 35243

tel 205.397.2100 | *fax* 205.397.2101

Board Certified: American Board of Surgery American Board of Plastic Surgery Cosmetic and Reconstructive Surgery of the Face, Breast, and Body

ATTACHMENT A

Guidelines For Nurse Injectors

INTRODUCTION

- The procedures of injecting neuromodulators and dermal fillers —is the practice of medicine in the state of Alabama.
- These are guidelines for delegating the procedures of injecting neuromodulators and dermal fillers. Nothing in these rules shall be construed to relieve the supervising physician of the professional or legal responsibility for the care and treatment of the physician's patients.

DEFINITIONS

- Direct Physician Supervision – Direct physician supervision shall mean that the physician is in the physical presence of the patient being treated and is directly observing a delegate's use of the modality.
- Level 1 Delegate – A Level 1 Delegate is an assistant to physicians (PA), a certified registered nurse practitioner, or registered nurse (RN) authorized in a written job description or protocol to administer injections of neuromodulators and dermal fillers, as designated in the written job description or protocol, and who has met the educational requirements for a Level 1 Delegate stated in Board rules.
- Site Supervision – On-site supervision means continuous supervision in which the supervising physician is physically present in the same building as the appropriate, properly trained Legal 1 Delegate who is injecting neuromodulators and/or dermal fillers. All treatments and procedures must be performed under the physician's direction and immediate personal supervision, and the physician must be immediately available at all times that the Level 1 Delegate is on duty. The physician retains full responsibility to patients and the Board for the manner and results of all services rendered.
- Remote Supervision – Remote supervision means proximity of a delegating physician to a Level 1 Delegate who is performing injections who is not providing on-site supervision but who is readily available for consultation, evaluation, referral, or direct medical intervention in person or by telemedicine. A remote physician's geographic physical proximity from the patient's treatment site must not exceed the ability of the physician to arrive on site the same day. Remote supervision may

only be provided by American Board of Medical Specialties or American Osteopathic Association board-certified physicians who have completed post-graduate training in injectables with such training meeting the standard of care as noted herein.

- Physician – A physician licensed by the Medical Licensure Commission of the State of Alabama.

DELEGATION AND SUPERVISION

- Delegating physicians must continually and regularly perform injectable services themselves as part of their primary practice.
- A physician holding an Alabama medical license who customarily performs the delegated medical service as part of his or her medical practice and not exclusively by delegating the service to an employee.
- A delegating physician must supervise the performance of all injectables by a Level 1 Delegate, including:
    - Ensuring that patients are adequately informed and, prior to treatment, have signed consent forms that outline Risks, Benefits, Alternatives, and Complications, including the disclosure of reasonably foreseeable side effects and complications that may result from the injectable treatment.
    - Ensuring that any Level 1 Delegate has read and signed the facility's policies and procedures, written protocols for delegation, and these rules regarding the safe use of injectables;
    - Prompt receipt of information from the Level 1 Delegate concerning any problem or complication encountered with any treatment;
    - On-site remote supervision for injectable treatments performed by Level 1 Delegates consistent with these rules, the training and experience of the delegate performing the procedure, and the risk of harm to the patient;
    - In person evaluation and care for complications that arise; and
    - Evaluation of the technical skills of the Level 1 Delegate performing injectable treatments on an ongoing basis by formally documenting and reviewing at least annually the Level 1 Delegate's ability to perform the following:

- To properly perform the injectable procedure and provide safe and effective care; and
- To respond appropriately to concerns, complaints, and complications and untoward effects of the procedures.

WRITTEN PROTOCOLS

"Written protocols" means a physician's order, standing delegation order, standing medical order, or other written order that is maintained on site.

A written protocol must be provided to the Board upon request and must provide, at a minimum, the following:

- A statement identifying the individual physician authorized to perform the injectable procedure and responsible for the delegation of the performance of the specified procedure, including proof of the physician's training in accordance with Board rules;
- A statement of the activities, decision criteria, and plan the Level 1 Delegate shall follow when performing delegated procedures;
- Selection criteria to screen patients for the appropriateness use of injectables;
- Identification of appropriate product to be used for patients who meet selection criteria;
- Methods by which the delegate plans to perform the medical injectable procedure;
- A description of appropriate care and follow-up for common complications, serious injury, or emergencies as a result of the injectable procedures;
- Procedures for obtaining proper consent forms signed by the patient or legal guardian;
- Instructions for maintaining a patient's chart, which should include, at a minimum, the patient intake form, the informed consent, the treatment sheet and progress notes, and before and after instructions;
- Instructions for documentation of a patient's treatment, decisions made, and a plan for communication or feedback to the authorizing physician concerning specific decisions made.
- Documentation shall be recorded within a reasonable time after each procedure and may be performed on the patient's record or medical chart; and
- Instructions to contact the supervising physician

immediately if complications or complaints from the patient arise.
- Written protocols should be signed by both the supervising physician and the corresponding Legal 1 Delegate.

INITIAL TRAINING REQUIREMENTS FOR PHYSICIANS AND DELEGATES

- These initial training requirements do not apply to any physician who holds a current board certification in the field of plastic surgery, facial plastic surgery, or dermatology.

Physicians and delegates involved in performing injectable treatments must meet the following training requirements before performing injectable procedures:

- Any physician where primary specialty training does not include the use of cosmetic injectables i.e. in Family Practice, OBGYN, General Surgery etc.
- A physician must complete thirty (30) hours of training.
- A Level 1 Delegate must complete forty (40) hours of training.
- Appropriate training for performing injectable treatments covered by this Chapter shall include the following topics:
  - Education in anatomical structures, such as nerves and blood vessels, that must be avoided when injecting neuromodulators and dermal fillers to minimize complications.
  - Eight (8) hours of injectable safety training, and
  - Two (2) hours of training on the Board's rules and regulations.

Appropriate training may be obtained through private courses, training on-site with a specialty board certified physician, physician-led training offered by product company. Documentation of training must be on file with Alabama Medical Board.

PROCEDURE REQUIREMENTS

Physicians and delegates involved in performing injectable procedures must complete a minimum number of procedure/product-specific training hours, a minimum number of observed procedures, a minimum number of supervised procedures, and a minimum number of cases under supervision as follows:

ATTACHMENT A

REMOTE PRACTICE SITE

- A remote practice site is a practice site at which a Level 1 Delegate may, if authorized by a written job description or collaborative protocol, perform injectable procedures under locally remote supervision.
- The physician shall initially examine the patient, either in person or by telemedicine (ZOOM), establish a treatment plan, obtain informed consent of the patient, and sign the patient chart prior to a Level 1 Delegate performing the first injectable procedure at a remote practice site.
- Subsequent treatments which are a continuation of a treatment plan documented in the patient's chart may be performed by the Level 1 Delegate at a remote practice site without examination of the patient by the physician before each treatment. If any changes are made to the treatment plan or the treatment plan ends, the physician must re-examine the patient prior to any updated treatment being performed.

ALTERNATE PHYSICIANS

- If a delegating physician will be unavailable to supervise a Level 1 Delegate as required by Board rules, arrangements shall be made for an alternate physician to provide that supervision.
- An alternate physician must have the same training in performance of injectable treatments as the primary supervising physician.
- Any alternate physician providing supervision shall affirm in writing to the Board of Medical Examiners that he or she is familiar with the protocols or standing delegation orders in use at the site, will be accountable for adequately supervising care provided pursuant to those protocols or standing delegation orders, and has the same training in performance of injectable treatments as the primary supervising physician.

QUALITY ASSURANCE

- The physician must ensure that there is a quality assurance program for the facility where injectable procedures are performed for the purpose of

continuously improving the selection and treatment of patients.

- An appropriate quality assurance program shall consist of the following elements:
  - A mechanism to identify complications and untoward effects of treatment and to determine their cause.
  - A mechanism to review the adherence of delegates to standing delegation orders, standing medical orders, and written protocols.
  - A mechanism to monitor the quality of injectable treatments.
  - A mechanism by which the findings of the quality assurance program are reviewed and incorporated into future standing delegation orders, standing medical orders, protocols, and supervising responsibility.
  - Ongoing training to improve the quality and performance of delegates.

REPORTING REQUIREMENT FOR ADVERSE EVENTS

Every physician who performs or supervises the performance of a procedure covered under these rules must report to the Board within three (3) business days the occurrence of all events related to a procedure that resulted in an emergency transfer of a patient to a hospital, unscheduled hospitalization related to the procedure, or death.

EFFECTIVE DATE

The deadline for compliance with the provisions of this section will be July 17, 2024.

CONTINUING EDUCATION AND MINIMUM ANNUAL PROCEDURES REQUIRED

- Level 1 Delegates must complete a minimum number of hours of continuing education and a minimum number of procedures to continue performing injectable procedures under these guidelines.
- Physicians are exempt from continued education and an annual minimum number of procedures but must maintain proper training on any procedure a Level 1 Delegate is allowed to utilize.

ATTACHMENT A

- If a delegate fails to meet these requirements, he or she must complete the initial training and procedure-specific training set forth in these guidelines.
- Level 1 Delegates must annually complete a minimum of four (4) hours of continuing injectable education.
- Continuing education may include AMA PRA Category 1 CME hours, injectable specific medical conference hours, online study and courses, and self-study through online webinars, lectures, CME courses, and hours lectured by a physician. Continuing injectable education obtained may be general for all injectable procedures and not specific to every procedure performed.
- Continuing education should include training on theory and physics; skin anatomy and conditions/diseases; product safety; treatment of conditions; recognition, management, and reporting of side effects and complications; and overall use of injectable procedures to treat patients.
- Level 1 Delegates must complete a minimum of ten (10) total injectable procedures per year.
- Level 1 Delegates must complete a minimum of ten (10) procedures in each procedure category they practice within, and Level 2 Delegates must complete a minimum of thirty (30) procedures in each procedure category they practice within.

ATTACHMENT B

Alabama Board of Nursing
Peggy Sellers Benson, RN, MSHA, MSN, NE-BC
Executive Officer

RSA Plaza, Suite 250
770 Washington Ave
Montgomery, AL 36104

www.abn.alabama.gov
(334) 293-5200
1-800-656-5318
Fax (334) 293-5201

Mailing address:
P.O. Box 303900
Montgomery, AL 36130-3900

November 18, 2024

E. Wilson Hunter, Esq.
General Counsel
Alabama Board of Medical Examiners
PO Box 946
Montgomery, Alabama 36101-0946
Via email: whunter@albme.gov

RE: Proposed Guidelines for Nurse Injectors

Dear Mr. Hunter:

Thank you so much for providing the Alabama Board of Nursing (ABN) with an opportunity to provide its thoughts regarding Dr. Core's request for ALBME to create delegation rules for the administration of neuromodulators and dermal fillers. The ABN members have authorized me to provide you with these comments.

We agree with Dr. Core's statement that "there is no data which supports the practice of cosmetic injectables being administered by non-physician injectors as unsafe," but we do not agree with the regulatory model imposed, because the ABN believes the injection of neuromodulators and dermal fillers constitutes the practice of nursing.

Dr. Core's document is entitled "Guidelines for Nurse Injectors." The introduction states that "[t]he procedures of injecting neuromodulators and dermal fillers – is the practice of medicine in the state of Alabama." ABN notes that ALBME previously had on its website a letter which stated: "The Board of Medical Examiners considers the procedures (Botox, Restylane, Collagen and Mesotherapy) to be the practice of medicine and as such each procedure must be performed by a licensed physician." That statement has now been removed, and according to the Executive Director of the Alabama State Nurses Association, a representative of the ALBME informed her that this statement was never an official opinion of the ALBME and there was no rule or statute that prevented the administration of minimally invasive cosmetic injectables by CRNPs.

ATTACHMENT B

In 2021, a CRNA requested a declaratory ruling from ABN asking whether it was within the scope of practice of a CRNA, a CRNP, or an RN to inject botulinum toxin into targeted sites of facial muscles for aesthetic maintenance and to perform the injection under medical direction of a physician licensed to practice medicine or a licensed dentist who has prescriptive authority. The ABN answered the question as to CRNAs and RNs.

The ABN noted:

> "Although the ABN certainly agrees that it could and, indeed, should be within the scope of practice for registered nurses who possess certificates of qualification to engage in advanced practice nursing and who have successfully completed graduate courses in health assessment, physiology/pathophysiology, and pharmacology, as well as an organized program of study and demonstrated competence, to administer botulinum toxin to patients for aesthetic or other purposes in a medical facility pursuant to an order from a legally authorized prescriber who has examined the patient, the ABN cannot issue a declaratory ruling to that effect, because doing so could expose the advanced practice nurse to injunctive proceedings pursuant to Code of Alabama § 34-24-52 or criminal consequences pursuant to Code of Alabama (1975), § 34-24-51, which states: "Any person who practices medicine or osteopathy or offers to do so in this state without a certificate of qualification having been issued in his or her behalf by the State Board of Medical Examiners and without a license and certificate of registration from the Medical Licensure Commission of Alabama shall be guilty of a Class C felony." That statement was based on the Alabama Board of Medical Examiners having stated in an October 21, 2004, letter the following: "The Board of Medical Examiners at its October 20, 2004 meeting considered your letter dated September 20, 2004. The Board of Medical Examiners considers the procedures (Botox, Restylane, Collagen and Mesotherapy) to be the practice of medicine and as such each procedure must be performed by a licensed physician."

As noted above, the ASNA Executive Director states she has been informed by an ALBME representative that the statement was never an official opinion of the ALBME and that there was no rule or statute that prevented the administration of minimally invasive cosmetic injectables by CRNPs.

ABN recognizes that the injection of neuromodulators/botulinum toxin A and dermal fillers requires understanding of the anatomy of the areas being injected and the medication/device being injected. RNs with advanced degrees are highly qualified from an educational standpoint to perform these injections, but other RNs may possess adequate educational backgrounds, augmented by course content, to enable the safe administration of these treatments.

ATTACHMENT B

In terms of an organized program of study, certainly the course content would need to include relevant anatomy and physiology, pharmacological aspects of the drug or substance being administered (to include possible side effects, adverse reactions, etc.), patient assessment and selection, contraindications for use, preparation of the substances (reconstituting, sterile technique, etc.), injection techniques, informed consent, and emergency measures to address adverse events. Supervised clinical practice would require that the RN perform a designated number of the procedures under the direct supervision of a prescriber trained in the procedure who will document the competence of the RN, initially and at periodic intervals. The standardized procedure application would have to contain all of this information.

It is important to remember that an RN may only perform these injections (or any other medical intervention) pursuant to an order from a lawful prescriber. Thus, any patient would have to have been assessed by a lawful prescriber who would prescribe the specific course of treatment for the RN to implement.

As Lawful Prescribers, CRNPs and CNMs in collaborative practice should be able to both order and administer neuromodulators/botulinum toxin A and dermal fillers.

Core skills for CRNPs and CNMs in collaborative practice include physical examinations and assessment, formulation of medical and nursing diagnoses, and instituting therapies. There is no reason why this authority should not encompass evaluating a patient for neuromodulators and dermal fillers, ordering those treatments, administering the medication according to the treatment plan, adjusting the treatment plan, and following up to evaluate treatment effectiveness and plan corrective measures in the event of adverse reactions. Regarding conducting the injections themselves, there is no reason to require a specialty protocol or skill request, because this is the practice of nursing and the CRNPs and CNMs may establish competence through the standardized procedure process, like any other RN.

Conclusion.

In conclusion, the ABN agrees that registered nurses who have completed an organized program of study, engaged in supervised clinical practice, and demonstrated clinical competence both initially and periodically, may inject neuromodulators/ botulinum toxin A and dermal fillers pursuant to an ABN-approved standardized procedures and an order from a lawful prescriber. ABN also agrees that as lawful prescribers, CRNPs should be able to evaluate patients and order treatment using neuromodulators/botulinum toxin A and dermal fillers, in addition to performing the injections. ABN believes this skill should be included on the standard protocol for CRNPs and CNMs for consideration by the collaborating physician and CRNP/CNM at the time of completing the collaborative practice application. It is neither necessary nor appropriate for ALBME to promulgate rules which purport to prescribe the training requirements for RNs and CRNPs/CNMs. Rules related to collaborative practice for

ATTACHMENT B

CRNPs and CNMs are initiated in the Joint Committee, and rules related to the scope of practice for RNs are the province of the ABN.

Please let us know if we may provide you with further information. We look forward to working with you as we work together to remove the barriers to practice which currently exist for our advanced practice nurses and registered nurses.

Sincerely,

Peggy Sellers Benson, RN, MSHA, MSN, NE-BC
Executive Officer

PSB/AMH/

ATTACHMENT C

ALABAMA DERMATOLOGY SOCIETY
Committed to Excellence in Dermatology for Alabama

P.O. Box 43212
Birmingham, Alabama 35243
www.alabamaderm.org

December 2, 2024

Alabama Board of Medical Examiners
Mr. William Perkins, Executive Director
848 Washington Ave,
Montgomery, AL 36104

Dear Distinguished Members of the Alabama Board of Medical Examiners,

We respectfully thank you for allowing us to comment upon the recent Guidelines for Nurse Injectors. **Our primary concern for patient safety prompts us to adamantly oppose any rule that allows nurse practitioners, nurses, or physician assistants to inject dermal fillers.**

Over the past 10 years, an increase in all dermal filler injections and related complications has been well documented in the literature [1-9]. The most serious of these are ischemic complications including tissue necrosis, stroke, blindness, and death [1-9]. As this phenomenon becomes better understood, it has become more important than ever for all injectors to have a detailed knowledge of injection anatomy, years of experience in dermal filler injection, and a keen understanding of the sometimes subtle presentation of an ischemic event. Injectors should possess the correct tools available to manage an emergency situation and a commitment to maintain an education in the latest literature in this rapidly changing landscape [18]. The most important factor in the ultimate outcome of these ischemic complications is the timeframe in which they are diagnosed and treated [16,17,18].

While medical spas and other non-physician offices provide easier access such as shorter wait times, lower prices, and a less rigorous clinical environment [15], these "clients" often become new patients to dermatologists when complications occur and cannot be managed properly by the original injector [11]. In fact, many patients with complications from injection visits never return to the provider that caused them, creating an ongoing perception of safety among inexperienced injectors [Zhou et al]. In addition, the companies that distribute dermal fillers have a vested interest in lowering the bar for entry into this field, lulling potential injectors and patients into a sense of comfort [13] and creating a perception that dermal fillers are safe [11,13]. Unfortunately, these complications have exponentially increased in incidence across the United States as non-physicians have gained the ability to inject. These emergency complications, when unrecognized and mishandled, result in much more morbidity and, in some cases, mortality than is acceptable.

Furthermore, the medical spa industry has not penetrated our state the way it has in others. If non-physicians become injectors, greedy investors will identify Alabama as a new investment opportunity. Medical spas, who are owned and operated by non-medical private equity investors, untrained physicians, physicians assistants, nurse practitioners, and nurses, will multiply in Alabama [medspa.org REF1]. If the only requirement for ownership is an MD, Alabama will experience the tragic "absent medical director" situation that occurs nationally. Investors will hire suboptimally trained individuals hoping to grow profits and "sell" in 3-4 years to large private equity groups for a lucrative payout. The fact that this market is untapped will make it very attractive for these undesirable groups.

ATTACHMENT C

Acting responsibly after this passed, Alabama would also need to put immediate rules in place for training, assessment of skill, testing of knowledge, continuing education for maintenance, complication monitoring, and adverse event accountability processes, as well as rules regarding the acquisition of injectable products (how and where they are acquired). This would be burdensome, expensive, extremely time-consuming, and difficult to enforce in a way that ensures the safety of patients. With no reporting rules, no requirement other than an MD to be a medical director, and no formal training program in place, Alabama is simply not ready to take this on. **It is of particular note that dermatologists in this state are not requesting that access be granted to non-physicians, even though there would be potential financial benefit to them.**

Like you all, our organization cares deeply about health disparities in Alabama, not Botox disparities. When we are not defending patient safety, our organization funds rural residency training, increases primary care access to dermoscopy, and provides sun shades to schools--to name a few. We are all painfully aware that Alabama ranks poorly among common indicators of public health such as life expectancy and obesity [U.S. Dept of Health, 2023]. Advanced practice providers often cite this need for increased access to primary care in their arguments for scope changes [Hudspeth et al]. We do not understand how this request achieves that goal and, further, we fear it will shunt advanced practice providers away from primary care and toward Medical Spas [medspa.org ref2].

As always, we remain committed to providing open conversation and to engaging in thoughtful and purposeful solutions in our collective priority of patient care and safety.

Respectfully,
Submitted by the Alabama Dermatology Society Leadership

References

Zhou, Albert E., et al. “Ethics of Dermatologists Having to Manage Cosmetic Complications by Other Clinicians.” Journal of the American Academy of Dermatology., 2024, https://doi.org/10.1016/j.jaad.2024.07.1465.
https://americanmedspa.org/blog/selling-your-medical-spa

National Vital Statistics Reports, Vol. 73, No. 7, August 21, 2024; Centers for Disease Control and Prevention. Adult Obesity Prevalence Maps. U.S. Dept of Health and Human Services; 2023

Hudspeth et al, Understanding Nurse Practitioner Scope…JAANP, August, 2019

https://americanmedspa.org/blog/private-equity-and-growth-capital-medical-aesthetics-new-reality

ATTACHMENT D

REVIEW ARTICLE

Avoiding and Treating Blindness From Fillers: A Review of the World Literature

KATIE BELEZNAY, MD, FRCPC, FAAD,* JEAN D. A. CARRUTHERS, MD, FRCSC, FRC (OPHTH), FASOPRS,† SHANNON HUMPHREY, MD, FRCPC, FAAD,* AND DEREK JONES, MD‡§

BACKGROUND As the popularity of soft tissue fillers increases, so do the reports of adverse events. The most serious complications are vascular in nature and include blindness.

OBJECTIVE To review the cases of blindness after filler injection, to highlight key aspects of the vascular anatomy, and to discuss prevention and management strategies.

METHODS A literature review was performed to identify all the cases of vision changes from filler in the world literature.

RESULTS Ninety-eight cases of vision changes from filler were identified. The sites that were high risk for complications were the glabella (38.8%), nasal region (25.5%), nasolabial fold (13.3%), and forehead (12.2%). Autologous fat (47.9%) was the most common filler type to cause this complication, followed by hyaluronic acid (23.5%). The most common symptoms were immediate vision loss and pain. Most cases of vision loss did not recover. Central nervous system complications were seen in 23.5% of the cases. No treatments were found to be consistently successful in treating blindness.

CONCLUSION Although the risk of blindness from fillers is rare, it is critical for injecting physicians to have a firm knowledge of the vascular anatomy and to understand key prevention and management strategies.

The authors have indicated no significant interest with commercial supporters.

Fillers have become an important treatment for patients who seek noninvasive rejuvenation. However, as the field of soft tissue augmentation becomes increasingly popular, reports of adverse events have increased. The most serious complications are vascular in nature and can lead to blindness. To highlight the significance of this issue, the Food and Drug Administration recently issued a safety communication about the risk of intravascular injection with soft tissue fillers.[1]

Having a thorough understanding of the vascular anatomy before injecting is critical. In this article, the authors review 98 cases of ocular complications secondary to soft tissue fillers and discuss the vascular anatomy and prevention and management strategies. To the knowledge of the authors, this is the largest review of blindness secondary to fillers in the literature.

Methods

A literature search was performed to gather information on ocular complications after injection of soft tissue fillers from reports published up to January 2015. The databases of the National Library of Medicine, Ovid MEDLINE, and Cochrane Library were searched using the following Boolean string: (soft tissue augmentation OR filler OR injectable) AND

*Departments of *Dermatology and Skin Science, and †Ophthalmology and Visual Science, University of British Columbia, Vancouver, British Columbia, Canada; ‡Skin Care and Laser Physicians of Beverly Hills; §Division of Dermatology, University of California at Los Angeles, Los Angeles, California*

ISSN: 1076-0512 • Dermatol Surg 2015;41:1097–1117 • DOI: 10.1097/DSS.0000000000000486

(blindness OR ophthalmoplegia OR vision OR visual impairment OR retinal artery occlusion OR ophthalmic artery occlusion). The search was limited to the English language literature. In addition, the references cited in the identified articles were reviewed to identify any additional reports. The review was limited to injected fillers and ocular complications.

Results

A total of 98 reports of filler-induced vision changes were identified. The data reported from the different studies were not consistent. The amount of the filler injected, injection technique, and needle type were reported in a minority of cases, and as such, this information was not included. This is likely due to the fact that often the physicians managing the blindness reported the cases as opposed to the injecting physician. A description of the cases, therapy, and outcomes are highlighted in Table 1.

Virtually Every Anatomic Location Where Filler is Injected on the Face is at Risk for Blindness

The most common sites for this complication were the glabella (38.8%, $n = 38$), nasal region (25.5%, $n = 25$), nasolabial fold (NLF) (13.3%, $n = 13$), and forehead (12.2%, $n = 12$) (Figure 1). Of the 25 nasal injections, 18 were listed as the nasal dorsum or nose, 1 was in the nasal tip, 4 were documented as lateral nasal or perinasal, 1 was in the septum, and 1 was in the nasal root. Moderate risk sites included the periocular region (8.2%, $n = 6$), temple (6.8%, $n = 5$), and cheek (6.8%, $n = 5$). However, although the cheek seems to be at a moderate risk, only 1 case occurred with injection at the cheek alone. Uncommon sites were the eyelid (4 cases), lips (3 cases), and chin (1 case). The exact anatomic location of injection was not listed in 5 cases. Although complications occurred when injecting at the lip and chin, it is important to note that these sites were not injected in isolation at the time of complication. Other anatomic sites that are at a higher risk, such as the NLF and nose, were injected at the same session and were therefore more likely to be the location of complication.

The fillers that caused blindness included: autologous fat (47.9%, $n = 47$), hyaluronic acid (HA) (23.5%, $n = 23$), collagen (8.2%, $n = 7$), paraffin (4.1%, $n = 4$), polymethyl methacrylate (3.1%, $n = 3$), silicone oil (3.1%, $n = 3$), poly-L-lactic acid (3.1%, $n = 3$), and calcium hydroxylapatite (2.0%, $n = 2$). There was one case each (1.4%) with injections from polyacrylamide hydrogel and micronized dermal matrix (Figure 2). The filler type was not reported in 4 cases. There were 8 cases of visual complications reported in the United States and 1 case reported in Canada. Most cases ($n = 58$) were reported out of South Korea. This could represent a reporting bias as many of the large case series are from South Korea. Data were collected from the major retinal centers in the country. To the knowledge of the authors, no similar data collection from ophthalmologists has been done in North America. There are limited data to assess whether the injection technique, needle or syringe type, or location of injection contribute to the higher number of cases of blindness seen in Korea. However, volumization of the diamond-shaped central portion of the face has become culturally popular in Korea; this area includes the glabella, nose, medial cheek, and NLF, all of which are high-risk sites for vascular occlusion of distal branches of the ophthalmic artery.

In 65 cases, complete unilateral vision loss was reported as the initial symptom or sign. In 41 cases, ocular pain or headache was reported. Nausea and vomiting were reported in 10 cases. Lack of extraocular movement or ophthalmoplegia was reported in 40 cases, ptosis in 32 cases, and exotropia, in which the eyes are deviated outward, in 16 cases. Although most cases of vision loss did not improve, only 2 patients had ongoing ophthalmoplegia, and 1 patient had persistent ptosis that was reported. Significant skin changes such as necrosis or a violaceous reticulated pattern were reported in 15 cases. Although a thorough review of neurological complications secondary to the filler was not undertaken, there were 23 cases (23.5%) of symptoms or signs involving the central nervous system (CNS), including infarction and hemiplegia in association with the cases of blindness. There was 1 case[14] of death in association with blindness after 5 mL of autologous fat was injected into the glabella. One minute after the injection, the patient developed mental status change; after 12 hours, she developed deep coma; and after 2 days, the left eye became necrotized. The patient died after 4 days.

ATTACHMENT D

TABLE 1. Cases of Blindness in the World Literature

Case	*Type of Filler*	*Injection Site*	*Symptoms*	*Signs*	*Management*	*Outcome (Variable Time for Follow-up)*	*Country*
1	Autologous fat	Glabella	Immediate: RE vision loss, hemicranial pain	NR	NR	RE vision loss	United States[2]
2	Autologous fat	Glabella	Immediate: RE vision loss, periocular pain	Paralyzed left limbs, left lower face hemiplegia, anosognosia, left spatial neglect, ↓ sensation on left	NR	RE vision loss, left-sided hemiplegia	Spain[3]
3	Autologous fat	Glabella	Immediate: RE vision loss, pain, vomiting	NR	NR	RE vision loss	Brazil[4]
4	Autologous fat	Left bridge of the nose, NLFs, lips	10 minutes: LE vision loss, eye and head pain, disoriented	Right-sided hemiparesis	NR	LE vision loss, neurologically normal, necrosis on the nose	United States[5]
5	Autologous fat	NLF	Immediate: LE vision loss, headache, dyspnea, irritability, near unconscious state	NR	Ocular massage, CO_2 and O_2 intermittently	LE vision loss, recovered mental status	Korea[6]
6	Autologous fat	Temple	RE vision loss, headache	Ophthalmoplegia, ptosis	NR	RE vision loss	China[7]
7	Autologous fat	Forehead	LE vision loss	Ophthalmoplegia, ptosis	NR	LE vision loss	China[7]
8	Autologous fat	Glabella, forehead	LE vision loss	NR	NR	LE vision loss	China[7]
9	Autologous fat	Forehead, temple	RE vision loss	Ophthalmoplegia, ptosis	NR	RE vision loss	China[7]
10	Autologous fat	Periorbital, cheek, nose, and lip	LE vision loss	Ophthalmoplegia, ptosis	NR	LE vision loss	China[7]
11	Autologous fat	Forehead, temple	RE vision loss, dizziness, vomiting	Ophthalmoplegia, ptosis	NR	RE vision loss	China[7]
12	Autologous fat	Temple	RE vision loss	Ptosis	NR	RE vision loss	China[7]
13	Autologous fat	Glabella	Immediate: RE vision loss, pain, nausea	NR	Drip infusion of urokinase, hyperbaric O_2, corticosteroid	RE vision loss	Japan[8]

ATTACHMENT D

TABLE 1. (Continued)

Case	Type of Filler	Injection Site	Symptoms	Signs	Management	Outcome (Variable Time for Follow-up)	Country
14	Autologous fat	NLF, lip, chin	No vision change, but multiple fat emboli in right retinal and choroidal arterioles	7 hours: global aphasia, mild right sensorimotor hemiparesis	NR	Ocular emboli no longer visible, aphasia	Switzerland[9]
15	Autologous fat	Forehead	Injection day: swelling, unable to open eyelids. Day 1: LE vision loss	Day 1: decreased sensation forehead, scalp, paresthesias right leg. Day 3: ophthalmoplegia, ptosis	IV methylprednisone for 3 consecutive days	LE vision loss, recovery of ophthalmoplegia	Korea[10]
16	Autologous fat	Periorbital area (crow's feet)	Immediate: LE weak reaction to light, pain, headaches, stuporous, unresponsive	Right hemiplegia, global aphasia, deviation of the head and eye to the left	NR	LE vision loss, recovery of ability to walk, improved global aphasia	Switzerland[11]
17	Autologous fat	Nose (left side)	Immediate: LE vision loss, pain	Ophthalmoplegia	Microcatheter at proximal ophthalmic artery with mechanical thrombolysis by rotating microwire, 500,000 U of urokinase and 500 μg of tirofiban infused	LE vision loss, recovery of ophthalmoplegia	Korea[12]
18	Autologous fat	Cheek	Vision loss	5 days later: vesicular lesion on ipsilateral nose	NR	Vision loss	NR[13]
19	Autologous fat	Transverse scar and wrinkle in the forehead	Immediate: vision loss, hemicranial pain	4 days later: superficial skin eruption forehead	NR	NR	NR[13]
20	Autologous fat	Glabella	30 minutes: LE vision loss	1 minute: mental change, aphasia, right hemiplegia. 30 minutes: drowsy, global aphasia, right sensorimotor hemiplegia. 12 hours: deep coma, central hyperventilation, decorticate rigidity. 2 days: necrotized left eye	Artificial ventilation, IV dexamethasone and saline	4 days later: death	Korea[14]

ATTACHMENT D

TABLE 1. (Continued)

Case	Type of Filler	Injection Site	Symptoms	Signs	Management	Outcome (Variable Time for Follow-up)	Country
21	Autologous fat	Glabella	24 hours: RE vision loss, ocular pain	NR	IV corticosteroids and antiplatelet therapy	RE vision loss	France[15]
22	Autologous fat	NLF	10 minutes: RE vision: hand motion	Ptosis, petechiae right NLF	IV methylprednisolone 1 g per day for 3 days followed by oral methylprednisolone	RE vision: hand motion	Korea[16]
23	Autologous fat	Forehead	Immediate: RE vision loss	NR	NR	NR	United States[17]
24	Autologous fat	Glabella	Immediate: LE vision loss, pain	Ophthalmoplegia, ptosis	Intra-arterial thrombolysis	LE vision loss	Korea[18]
25	Autologous fat	NLF	Immediate: LE vision loss, pain	Ophthalmoplegia, exotropia	Intra-arterial thrombolysis	LE vision loss	Korea[18]
26	Autologous fat	NLF	Immediate: RE vision loss, pain	Ophthalmoplegia, ptosis, esotropia	Intra-arterial thrombolysis	RE vision loss	Korea[18]
27	Autologous fat	Glabella	1 week: LE vision loss, pain	Ophthalmoplegia, ptosis, exotropia, MCA infarction	NR	LE vision loss	Korea[18]
28	Autologous fat	Glabella	Immediate: RE vision loss, pain	Ophthalmoplegia, exotropia	Anterior chamber paracentesis	RE vision loss	Korea[18]
29	Autologous fat	Glabella	2 hour: LE vision loss, pain	Exotropia	Anterior chamber paracentesis	LE vision loss	Korea[18]
30	Autologous fat	Glabella	2 days: LE vision: light perception	2 days: ACA and MCA infarction	Anterior chamber paracentesis	LE vision: light perception	Korea[18]
31	Autologous fat	Periocular	After effect of anesthesia: LE vision loss	2 hours later: dysarthria, purple discoloration to nose, MCA infarction	Ocular massage, IV mannitol, O_2 and CO_2 therapy	LE vision loss	Korea[19]
32	Autologous fat	Face	13 hours: RE vision loss, left hemiplegia, right-sided facial palsy	Multiple brain infarctions	IV methylprednisolone (9 mg/kg) followed by prednisolone (30 mg/kg) taper	NR	Korea[20]
33	Autologous fat	Left face	10 minutes: LE vision loss, headache	Decreased cognition, multiple bilateral infarcts	NR	NR	Korea[21]

ATTACHMENT D

TABLE 1. (Continued)

Case	Type of Filler	Injection Site	Symptoms	Signs	Management	Outcome (Variable Time for Follow-up)	Country
34	Autologous fat	Glabella	RE vision loss, LE: 20/130 (0.15)	Right ophthalmoplegia, ptosis, red reticular pattern on the glabella and necrosis, infarction bilateral frontal lobes	NR	RE vision loss, exotropia, LE vision: 20/20, minimal scarring	Korea[22]
35	Autologous fat	NR	Within 1 day: RE vision: light perception, pain	Ophthalmoplegia, exotropia	Observation	RE vision loss	Korea[23]
36	Autologous fat	Glabella	Within 1 day: RE vision loss	Ophthalmoplegia, ptosis, exotropia, border-zone infarct in the brain	Intraocular pressure lowering	RE vision loss	Korea[23]
37	Autologous fat	Glabella, NLF	Within 6 hours: LE vision loss	Ophthalmoplegia, MCA infarct	Anterior chamber paracentesis	LE vision loss	Korea[23]
38	Autologous fat	NR	Within 1 day: LE vision loss, pain	Ophthalmoplegia, border-zone infarct in the brain	Observation	LE vision loss	Korea[23]
39	Autologous fat	NR	Within 8 hours: LE vision: counting fingers	NR	Anterior chamber paracentesis	LE vision loss	Korea[23]
40	Autologous fat	Glabella	Within 4 hours: LE vision loss, pain	Ophthalmoplegia, ptosis	Anterior chamber paracentesis	LE vision loss	Korea[23]
41	Autologous fat	Glabella	Within 1 day: RE vision loss	Multifocal brain infarcts	Anticoagulant	RE vision loss	Korea[23]
42	Autologous fat	Glabella	Within 30 hours: RE vision: light perception	Ophthalmoplegia, ptosis, MCA infarct	Anterior chamber paracentesis	RE vision loss	Korea[23]
43	Autologous fat	Glabella, NLF	Within 2 hours: LE vision loss, pain	NR	Observation	LE vision loss	Korea[23]
44	Autologous fat	NLF	Within 1 day: LE vision loss	Multifocal brain infarcts	Intraocular pressure lowering	LE vision loss	Korea[23]
45	Autologous fat	Nasal dorsum	Within 1 day: LE vision: 20/25	Ophthalmoplegia	Observation	LE vision: 20/50	Korea[23]
46	Autologous fat	Eyelid	Within 1 day: RE vision: 20/25	NR	Anticoagulant	RE vision: 20/40	Korea[23]
47	Autologous fat	Glabella	Within 1 day: LE vision loss	Ophthalmoplegia, exotropia	Observation	LE vision loss	Korea[23]

ATTACHMENT D

TABLE 1. (Continued)

Case	Type of Filler	Injection Site	Symptoms	Signs	Management	Outcome (Variable Time for Follow-up)	Country
48	HA	Glabella, cheeks	1 minute: vision loss in the inferior half of the RE	NR	Immediate: 500 mg acetazolamide	RE vision recovery, visual field defect improved	Germany[24]
49	HA	Nasal tip	Immediate: LE vision loss, pain in the left upper face	Day 2: violaceous, reticulated, ulcerative patches, ophthalmoplegia	Day 2: IV methylprednisolone ×3 days, then tapered oral prednisolone; aspirin 100 mg orally	LE vision loss; recovery from ophthalmoplegia and skin necrosis	Korea[25]
50	HA	Nose	LE vision: 20/400, headache	NR	NR	LE vision: 20/1,000	China[7]
51	HA	Periorbital	RE vision counting fingers 33 cm	NR	NR	RE vision counting fingers 33 cm	China[7]
52	HA	Forehead	LE vision hand movement	NR	NR	LE vision: 20/1,000	China[7]
53	HA	Upper eyelid	LE vision loss, dizziness, vomiting	Ophthalmoplegia, ptosis	NR	LE vision loss	China[7]
54	HA	Nose	RE vision loss, dizziness, vomiting	Ophthalmoplegia, ptosis	NR	RE vision loss	China[7]
55	HA	Nasal dorsum	Immediate: RE vision loss, periocular pain	Ophthalmoplegia, ptosis	High-dose IV corticosteroids	RE vision loss, ophthalmoplegia	Korea[26]
56	HA	Forehead	3 weeks: LE vision: 20/30, superior field vision loss	NR	NR	LE vision: 20/25	United States[17]
57	HA	NLF and glabella	Immediate: RE vision loss, pain	Ophthalmoplegia, ptosis, exotropia	Intra-arterial thrombolysis	RE vision loss	Korea[18]
58	HA	NLF	2 weeks: LE vision: 20/20 (1), inferior visual field defect	NR	NR	LE vision: 20/20 (1), no comment on visual field defect	Korea[18]
59	HA	Glabella	5 hours: LE vision: 20/30 (0.7), inferior visual field defect	NR	Massage, anterior chamber paracentesis	LE vision: 20/130 (0.15)	Korea[18]

ATTACHMENT D

TABLE 1. (Continued)

Case	Type of Filler	Injection Site	Symptoms	Signs	Management	Outcome (Variable Time for Follow-up)	Country
60	HA	NLF	3 weeks: RE vision: 20/20 (1), inferotemporal visual field defect	NR	NR	RE vision: 20/20 (1), no comment on visual field defect	Korea[18]
61	HA	Nose	Immediate: RE vision loss, pain, drowsiness	Paralysis of the right face and left limbs. MCA infarction with intracerebral hemorrhage, SAH	Thrombolysis, decompressive craniectomy	RE vision loss, motor weakness (walks with a cane), drowsiness	Korea[27]
62	HA	Nasal dorsum	Immediate: RE vision: 20/63 (0.3), pain, nausea, vomiting, headache. Few seconds: diplopia, dizziness	Ophthalmoplegia, ptosis, exotropia. Ecchymosis, reticulated discoloration, swelling forehead and nasal dorsum	Aspirin, "nicergorline," eye drops, systemic steroid pulse therapy for 3 days, then oral steroids. Hyaluronidase to skin lesions, topical antibiotic, IV antibiotics	RE vision: 20/32 (0.6), recovery of ptosis, strabismus, ophthalmoplegia, diplopia. Minimal skin blemish	Korea[28]
63	HA	Glabella	Few minutes: vision loss, pain, headache. Exam: RE vision loss, LE vision: 20/25 (0.8)	Erythematous violet reticular discolouration in the glabella. Infarction right frontal, occipital, parietal lobes	Topical timolol maleate, oral acetazolamide (500 mg), aspirin 100 mg daily	Vision loss RE, left hemianopia	Taiwan[29]
64	HA	Glabella	Within 1 hour: LE vision loss, pain	Ophthalmoplegia, ptosis, exotropia	Anterior chamber paracentesis	LE vision loss	Korea[23]
65	HA	Glabella	Within 7 hours: RE vision loss	NR	Intra-arterial thrombolysis	RE vision loss	Korea[23]
66	HA	NLF	Within 20 hours: RE vision: hand motion, pain	Ophthalmoplegia, ptosis, exotropia	Anterior chamber paracentesis	RE vision: 20/25	Korea[23]
67	HA	Glabella	Within 3 hours: LE vision: 20/32	Ophthalmoplegia, ptosis, exotropia	Anticoagulant	LE vision: 20/25	Korea[23]
68	HA	Glabella	Within 2 days: RE vision: 20/200	NR	Observation	RE vision: 20/63	Korea[23]
69	HA	Glabella	Within 5 hours: RE vision: 20/500	NR	Anterior chamber paracentesis	RE vision: 20/100	Korea[23]

ATTACHMENT D

TABLE 1. (Continued)

Case	Type of Filler	Injection Site	Symptoms	Signs	Management	Outcome (Variable Time for Follow-up)	Country
70	HA	Glabella, nasal dorsum	Within 4 hours: RE vision: light perception, pain	Ophthalmoplegia, ptosis, exotropia	Observation	RE vision: light perception	Korea[23]
71	Collagen (Zyderm)	Glabella and cheek (acne scars)	Within minutes: vision loss	NR	NR	Vision loss	NR[30]
72	Collagen	Glabella	NR	NR	NR	NR	United States[31]
73	Collagen	Glabella, cheeks	NR	NR	NR	Vision loss	NR[32]
74	Collagen	Left nasal septum	Immediate: LE vision loss, headache	Reticulated violaceous pattern nose, supraorbital area, forehead and philtrum, ptosis, ophthalmoplegia, acute cerebral infarction, and SAH	Antiplatelet agent, calcium channel blocker	LE vision loss	Korea[33]
75	Bone collagen	Nose	RE vision loss	Ophthalmoplegia, ptosis	NR	RE vision loss	China[7]
76	Collagen	Glabella	1 hour: LE vision: counting fingers	NR	Massage, mannitol	LE vision: 20/63 (0.3)	Korea[18]
77	Collagen	Nasal dorsum	Within 3 days: LE vision: 20/1,000	NR	Observation	LE vision: 20/200	Korea[23]
78	Paraffin	Nose	Immediate: vision loss	NR	NR	NR	United States[34]
79	Paraffin	Forehead	Immediate: RE vision loss	NR	NR	NR	Korea[15]
80	Paraffin	Nose	Immediate: vision loss, vomiting, collapse	NR	NR	NR	NR[34]
81	Paraffin	Nose	Immediate: LE vision loss, lacrimation, vertigo	NR	NR	NR	NR[34]
82	PMMA	Glabella	Immediate: RE vision loss, pain	Ophthalmoplegia	None	RE vision loss, ophthalmoplegia	Brazil[35]
83	MetaCrill (PMMA)	Nasal dorsum	15 minutes: RE vision: hand motion, pain	Ophthalmoplegia, ptosis	NR	RE vision loss, recovery from ophthalmoplegia and ptosis	Japan[36]

ATTACHMENT D

TABLE 1. (Continued)

Case	Type of Filler	Injection Site	Symptoms	Signs	Management	Outcome (Variable Time for Follow-up)	Country
84	Bovine collagen and PMMA (ArteFill)	Forehead	Immediate: RE vision loss	NR	Anterior chamber paracentesis, IV normal saline, ocular massage, hyperbaric O_2	RE vision: faint light perception	United States[17]
85	Silicone oil	Nasal root	Immediate: RE vision: counts fingers, pain	NR	Digital massage, vasodilators, acetazolamide	RE vision: counts fingers	Korea[37]
86	Silicone oil	Nose	1 day: LE vision loss	1 day: right hemiplegia	NR	NR	Korea[15]
87	Silicone oil	Temple	Immediate: RE vision loss, pain, headache	NR	Ocular massage, anterior chamber paracentesis, oral acetazolamide	RE vision loss	Thailand[15]
88	PLLA	Periorbital and lateral nasal area	Immediate: LE vision loss, pain. Day 2: nausea	Day 2: ophthalmoplegia, ptosis	NR	LE vision: decreased light perception and projection; recovery from ophthalmoplegia and ptosis	Canada[38]
89	PLLA	Eyelid	Within 3 hours: RE vision: light perception, pain	Ophthalmoplegia, exotropia	Observation	RE vision loss	Korea[23]
90	PLLA	Glabella	Within 1 day: LE vision: hand motion	NR	Steroid	LE vision: hand motion	Korea[23]
91	CaHA	Nasal dorsum	Immediate: RE pain. 8 hours: RE vision: hand movement	Ophthalmoplegia, ptosis, exotropia. Late: necrosis and reticulated erythematous-patterned glabella, nasal bridge and right eyelid	Immediate: aspiration. Later: topical and IV antibiotics, oral corticosteroids	RE vision recovery, fixed dilated pupil, minimal scarring	Korea[39]
92	CaHA	Nose	Vision loss bilateral	Bilateral ptosis, ophthalmoplegia, skin necrosis, red reticular pattern affecting the bridge of the nose and frontal area	NR	Vision loss bilateral	Korea[40]

TABLE 1. (Continued)

Case	Type of Filler	Injection Site	Symptoms	Signs	Management	Outcome (Variable Time for Follow-up)	Country
93	Polyacrylamide hydrogel (Aquamid), botulinum toxin Type A	NR, likely periocular	Immediate: nausea, vomiting. Left upper eye visual field defect for 3 days when reported. LE vision: 20/70	Ophthalmoplegia, ptosis, transient third nerve palsy. Edema, erythema, pustules, and cellulitis from glabella to nasojugal folds	Oral steroids, IV antibiotics, aspirin	LE vision: 20/30 with superior half visual field defect	Taiwan[41]
94	Cymetra (micronized dermal matrix)	Forehead (depressed scar)	10 minutes: nausea, diaphoresis. Subsequent: LE pain. 30 minutes later: LE vision: hand motion	Ptosis, exotropia	NR	LE vision: light perception, hypertropia, exotropia	United States[42]
95	NR	Glabella	Immediate: vision loss	Subsequent necrosis to the glabella	NR	NR	NR[43]
96	NR	Glabella, perinasal, periorbital	Immediate: LE vision loss	Erythema to injection sites	Acetazolamide (1 week), IV methylprednisolone (3 days)	Vision: 20/200	Korea[44]
97	NR	Nasal dorsum	Within 1 day: LE vision: 20/32	NR	Intraocular pressure lowering	LE vision: 20/20	Korea[23]
98	NR	Eyelid	Within 2 days: RE vision: 20/20	NR	Anticoagulant	RE vision: 20/20	Korea[23]

CaHA, calcium hydroxylapatite; CO_2, carbon dioxide; LE, left eye; MCA, middle cerebral artery; NR, not reported; O_2, oxygen; PLLA, poly-L-lactic acid; PMMA, polymethyl methacrylate; RE, right eye; SAH, subarachnoid hemorrhage.

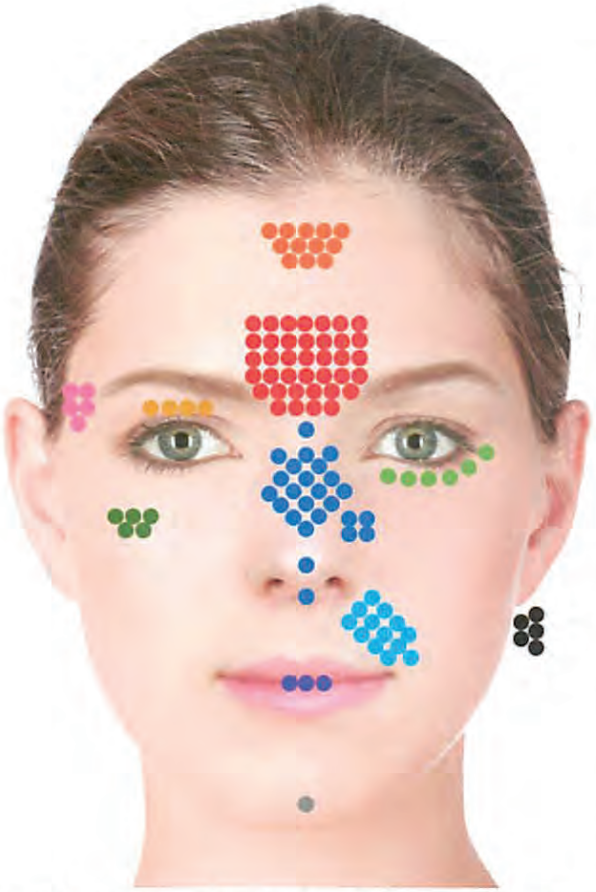


Figure 1. Location of injection for each case of blindness from filler. The 5 black dots represent cases in which the location was not specified and listed as "face."

The most serious complications were secondary to autologous fat. In this series, 38/47 or 80.9% of the cases of ocular complications from autologous fat resulted in complete vision loss, 4 cases did not report a final vision outcome, and 5 cases had some vision ranging from light perception to 20/40 at follow-up; 19/23 or 82.6% of the cases of CNS complications seen in association with blindness were secondary to autologous fat. Hyaluronic acid injections did not have such serious ocular outcomes. Vision loss was seen in 9/23 or 39.1% of the cases of ocular complications from HA. Some degree of vision ranging from counting fingers to full vision was seen in the remaining 14 cases. CNS complications in association with vision changes after HA injection were seen only in 2 cases.

Treatment varied from observation to digital massage, intraocular pressure-lowering agents such as acetazolamide and mannitol, intravenous (IV) methylprednisolone oral corticosteroids, oxygen and carbon dioxide therapy, antibiotics, mechanical and chemical thrombolysis, anterior chamber paracentesis, or anticoagulants. Hyaluronidase was injected to the skin at signs where signs of vascular compromise were present in one case. In many cases, treatments were not reported. The authors suspect that in these cases no treatment was instituted in large part because there is little evidence for improvement with any one treatment. Given the lack of consistent reporting on treatment, it is difficult to make any correlation between treatment and symptom improvement or resolution. In this review, there were only 2 cases that had complete vision recovery. In 1 case[22] of bilateral ocular complications, there

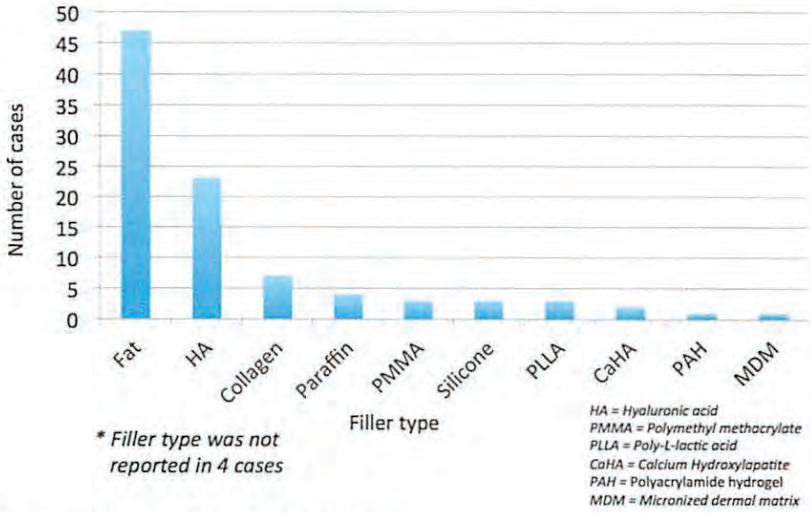


Figure 2. Number of cases of blindness from each filler type.

was resolution of the vision defects in the left eye, but vision loss in the right eye persisted.

Discussion

Background

The increasing demand for soft tissue fillers has been well documented. Similarly, the number of reported cases of vascular complications secondary to fillers is rising.[45] This could be secondary to a number of issues. First, there are increasing numbers of filler treatments being performed and risks would parallel this. Second, there has been a shift from 2-dimensional treatment of discrete wrinkles toward 3-dimensional panfacial volume restoration to achieve improved esthetic results. In such a scenario, larger volumes of filler are often placed in a deeper plane for revolumization. The combination of larger volumes and deeper placement increases the risk of blood vessel compromise. Last, there is a concern that nonexpert injectors are injecting fillers without a proper understanding of facial anatomy, thereby increasing the risk of complications. Between 1906 and 2015, 98 cases of blindness were documented in the literature with most cases being reported in the last 5 years. In 2014 alone, there were 5.5 million filler treatments performed worldwide, with that number forecasted to grow.[46] Thus, although blindness is a devastating complication, the risk is still exceedingly low.

Proposed Mechanism

With the rising reports of blindness secondary to soft tissue augmentation, the understanding of the mechanism of this complication has evolved. It has been suggested that vascular complications such as blindness can be attributed to intravascular injection and retrograde embolization of the filler.[47] Although it may seem logical that the material injected into an artery would flow in the direction of blood flow, in fact, the arteries branch and become smaller more distally, which increases resistance. A rapidly injected bolus may find less resistance proximally than distally. It has been shown that arterial pressure can be easily overcome when injecting and the material can travel in a retrograde fashion.[48] Multiple branches of the ophthalmic artery project outside the ocular area and onto the nose and forehead. Proximal branches include the supraorbital, supratrochlear, and dorsal nasal artery. Furthermore, there are anastomoses between many other arteries of the face and those branches of the ophthalmic artery. If the tip of the needle or cannula penetrates the vessel and enough pressure is applied to the plunger when injecting even small volumes of filler, the arterial pressure can be overcome and the filler can reach the ocular vessels. When the injector stops the pressure of injection, the arterial pressure can carry the embolus from the proximal vessels such as the ophthalmic artery to the more distal retinal arteries. Because these are small arteries, a large volume of filler is not required to cause occlusion. Indeed, many of the reported cases have involved injections of 0.5 mL or less.[48] If the injector applies greater pressure for longer, there is a chance that the filler may travel retrograde into the internal carotid artery and from there may advance into the cerebral circulation, causing a stroke.[47]

Anatomy

A firm understanding of anatomy is critical to minimize the risks of vascular complications. Most of the blood supply to the face is through the external carotid artery with the exception of a region of the central face that encompasses the eye, upper nose, and central forehead. The ophthalmic artery of the internal carotid provides blood supply to this area.[49] The ophthalmic artery arises behind the eye and branches into vessels including the supraorbital, supratrochlear, dorsal nasal, and lacrimal artery. These arteries are the most likely implicated in cases of vascular complications when injecting the glabella, nose, and forehead. The internal carotid system also anastomoses with branches of the external carotid system.[50]

The facial artery branches off the external carotid artery. It passes over the face anterior to the masseter muscle and proceeds with a tortuous course in a superior and diagonal direction. It gives rise to the inferior and superior labial arteries. The lateral nasal artery (LNA) branches off the facial artery to supply the lateral nose. The exact course of the facial artery as it courses superiorly is variable. Traditionally, the

facial artery becomes known as the angular artery (AA) in the region of the NLF. As the AA continues superiorly, it anastomoses with the dorsal nasal artery connecting the external and internal carotid systems. This anastomosis is the reason that injections in the NLF, medial cheek, or periorbital area can lead to blindness. The facial artery also anastomoses with the infraorbital artery and the transverse facial artery, a branch of the superficial temporal artery.[50] In this section, the cutaneous vascular anatomy of at high-risk anatomic sites of injection is reviewed (Figure 3).

Glabella and Forehead

The most likely arteries to cause complications secondary to soft tissue augmentation in the glabellar and forehead regions are the supratrochlear and supraorbital artery. Both these arteries are branches of the ophthalmic artery. As such, filler placed intravascular into one of these arteries with enough pressure can travel retrograde and lead to ocular complications. The supratrochlear artery is found to be relatively constant along the medial canthal vertical line. It rarely deviates more than 5 mm lateral or medial from this vertical line. It starts its course deep at the superomedial orbit and then becomes subcutaneous from 15 to 25 mm above the supraorbital rim as it travels superiorly. The supraorbital artery appears over the supraorbital rim on a vertical line corresponding to the medial limbus of the cornea. It also starts its course deep and becomes more superficial approximately 15 to 20 mm above the supraorbital rim and remains subcutaneous as it travels superiorly up the forehead. As such, injections at the glabella or inferior forehead at the level of the supraorbital rim or within 2 cm of that location should be superficial. However, injections more superiorly on the forehead should be deep in a supraperiosteal plane to avoid intravascular injection.[51]

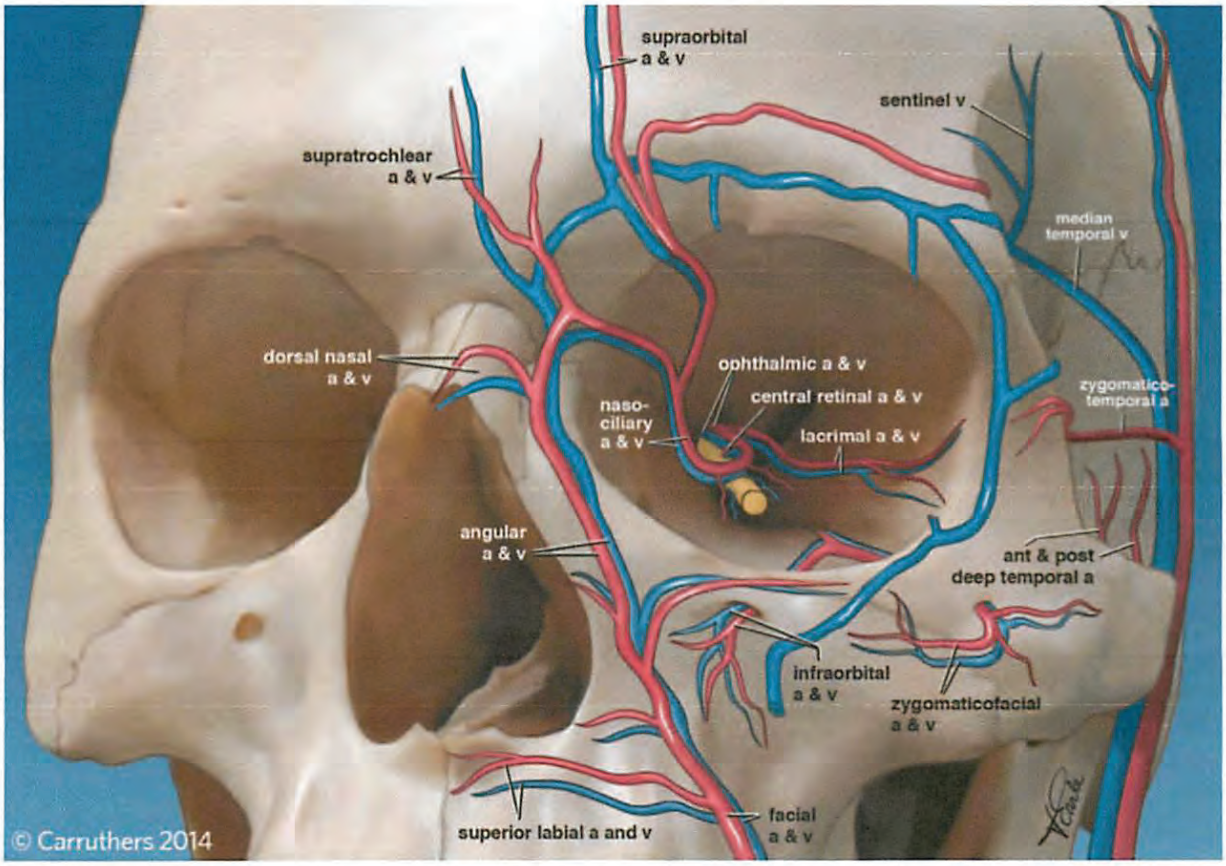


Figure 3. Vascular anatomy of the upper face (Copyright Jean D. Carruthers, MD, 2014).[47] a, artery; v, vein. Adaptations are themselves works protected by copyright. So in order to publish this adaptation, authorization must be obtained both from the owner of the copyright in the original work and from the owner of copyright in the translation or adaptation.

Nose

The major nasal arteries at risk for complications are the LNA and dorsal nasal artery. However, there are many small arteries and several anastomoses in the nasal region. In most cases, the LNA provides the main blood supply to the tip, and the dorsal nasal artery is the main supplier to the upper portion of the nose. The dorsal nasal artery can be identified usually 5 mm above the medial canthal horizontal line.[51] The main arteries anastomose connecting the external and internal carotid systems at the level of the superficial musculoaponeurotic system (SMAS) plane and above. The presence of so many anastomotic vessels in the nasal area, whose blood flow can be easily reversed with injections, creates risk of embolism when injecting fillers. When injecting filler in the nose, the filler is most safely placed in the avascular deep supraperiosteal plane below the nasal SMAS. If the patient has had previous surgical treatments on the nose, filler injections are not advised or should be performed with extreme caution with the risks extensively reviewed with the patient.[52]

Nasolabial Fold/Medial Cheek/Periorbital Region

The most likely blood vessel at risk for compromise in the medial cheek, NLF, and medial periorbital area is the AA. A recent study by Kim and colleagues describes 4 patterns of the AA (Figure 4). In Type I (19.3%), the AA originates from the branching point of the LNA adjacent to the ala of the nose and continues superiorly to the forehead. In Type II (31.6%), the AA originates from the facial artery near the mouth corner, proceeds to the infraorbital area, and then courses medially along the nasojugal and medial canthal areas. In Type III (22.8%), the AA originates from the ophthalmic artery at the medial canthal area. In Type IV (26.3%), the facial artery terminates as the LNA without producing an AA branch. Given the variable pattern, care must be taken when injecting the medial cheek, tear trough, or NLF as the AA can be present at these sites.[53]

The depth of the facial artery and its branches varies. Lee and colleagues[54] studied 54 cadavers to examine the relationship between the facial artery and facial muscles. They found 3 different branching patterns of the facial artery, which parallel the findings of the study by Kim and colleagues; however, the proportions varied. In the study by Lee and colleagues, the Type I pattern or nasolabial pattern was the most common with 51.8% of cadavers having the facial artery ascend along the lateral side of the nose. This pattern reflects the typical description in anatomy textbooks.[54] Lee and colleagues went further and described the depth of the facial artery and its branches. In the region of the NLF between the mouth corner and nasal ala, the facial artery branches were located in the subcutaneous layer on the surface of the facial muscles in 85.2% of cases. Therefore, injection in the NLF is best placed in a more superficial plane, that is, dermal or immediately subdermal. In addition to the NLF, the vessels are commonly located in a subcutaneous plane lateral to the mouth corner at the modiolar region and lateral to the nasal ala. If present, the infraorbital branch seen in Type II is also commonly seen in a subcutaneous plane.[54] The key message from both of these studies is that the AA may be located in the medial cheek/infraorbital area and that the facial artery and its branches may be in the subcutaneous plane, making intravascular injection a risk factor when injecting in this plane.

There are other important cutaneous arteries in the cheek region. The infraorbital artery is a branch of the maxillary artery and is located in the region of the medial cheek. It anastomoses with the facial artery and the dorsal nasal branch of the ophthalmic artery.[55] The lacrimal artery branches into the zygomaticofacial artery and zygomaticotemporal artery. The zygomaticofacial artery passes through the lateral wall of the orbit and emerges to supply the skin overlying the cheek prominence. Both the zygomaticofacial and infraorbital arteries connect with the ophthalmic artery either directly or through anastomoses. The zygomaticotemporal artery also passes through the lateral wall of the orbit and contributes to the blood supply of the temple in addition to the arteries highlighted in the next section.[56]

Temple

The lateral face, scalp, and forehead are primarily supplied by the superficial temporal artery and its branches. This artery begins in the superficial lobe of the parotid gland as the terminal branch of the external

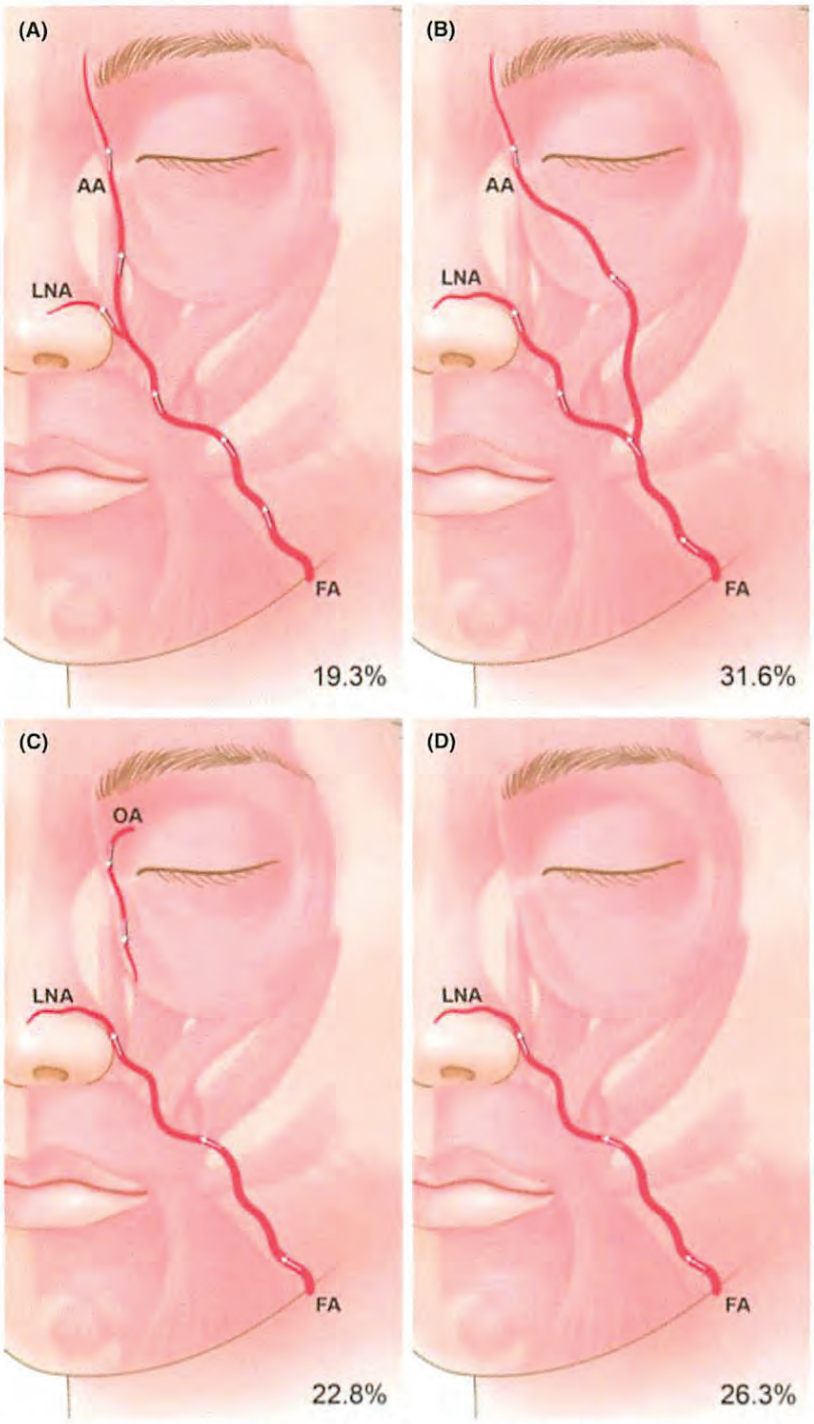


Figure 4. Schematic illustrations showing the 4 patterns of the AA. (A) Type I, the persistent pattern in which the AA originates from the branching point of the LNA from the facial artery (FA) adjacent to the ala of the nose. (B) Type II, the detouring pattern in which the AA traverses continuously from the detouring branch of the FA and ascends vertically to the nasojugal and medial canthal areas. (C) Type III, the alternative pattern in which the AA originates only from the ophthalmic artery. (D) Type IV, the latent pattern in which the FA terminates around the nasolabial area without giving off an AA branch. The arrows indicate the blood flow route in the arteries (Copyright Hee-Jin Kim, DDS, PhD, 2014).[53] Adaptations are themselves works protected by copyright. So in order to publish this adaptation, authorization must be obtained both from the owner of the copyright in the original work and from the owner of copyright in the translation or adaptation.

carotid artery. It gives off the transverse facial artery, which runs parallel to and 2 cm below the zygomatic arch. This branch anastomoses with the facial artery. At the superior border of the zygomatic arch, the superficial temporal artery gives off a second branch, the middle temporal artery. From there, the superficial temporal artery continues superiorly and branches into the anterior or frontal branch and parietal branch just above the level of the ear. As the frontal branches of the superficial temporal artery move medially, they become more superficial up to a subdermal level.[51] There are many anastomoses on the scalp between the bilateral superficial temporal arteries and the supraorbital and supratrochlear arteries, which could contribute to vascular complications.[49] However, ocular complications when injecting in the temple may result from injection into the middle temporal vein (MTV). The MTV is connected to the cavernous sinus through the periorbital veins, and it has been hypothesized that it may be easier for filler to be inadvertently injected into the MTV, which is much larger than similar arteries in that area, leading to cavernous sinus embolization. The authors suggested that the safest area to inject filler in the temple is 1 fingerbreadth above the zygomatic arch as the MTV was not found in that area. In addition, it is recommended that filler be placed in a supraperiosteal plane rather than subcutaneously as the MTV is located more superficially.[57]

Eyelid

The vascular supply of the eyelids is complex and is derived from anastomoses between the internal and external carotid arteries. The medial and lateral palpebral arteries directly supply the lid with contributions from many different vessels including the ophthalmic, facial, superficial temporal, and infraorbital arteries. The rich anastomoses between the vessels can lead to embolic material reaching the ophthalmic artery, and as such, caution must be taken when injecting in the thin skin of the eyelid.[49]

Clinical Features

Most commonly, ocular symptoms occurred immediately after injection. Vision loss, ocular pain, and headache were the most common symptoms. Nausea and vomiting, secondary to increased intraocular pressure, were reported in 10 cases. Variable ocular signs were reported. Paralysis of the eye muscle resulting in ophthalmoplegia occurred in 40 cases, and ptosis was seen in 32 cases. Obstruction of the blood supply to the extraocular muscles or innervating nerves causes ophthalmoplegia. Ptosis results from the lack of blood supply to the levator palpebral muscle or its innervating nerves.[18] Although vision recovery was rare, ophthalmoplegia and ptosis recovered in the majority. This is likely because nerves and muscles regenerate after vascular compromise, whereas the retinal damage is irreversible after 90 minutes.[15] Skin changes along the path of the vessel where the vascular occlusion occurred were seen in 15 cases. Typically, this presented as a violaceous reticulated pattern, and occasionally necrosis.

Autologous fat was the filler type most likely to cause visual complications. This could reflect use of larger volumes, larger syringes, and higher extrusion pressures. A review of the 47 cases of blindness resulting from injection of fat found that only a few articles reported procedural details. In these cases containing more detailed information, a range of syringe sizes were used from 10 to 20 mL, the needle or cannula size ranged from 0.3 to 2 mm in diameter or 23 to 12 gauge, and the injection volume of fat ranged from 2 to 20 mL. The lack of consensus with regard to the technique and regional differences may have also contributed to safety outcomes. Autologous fat had a higher risk of permanent vision loss as the ultimate ocular outcome at 80.9% compared with HA at 39.1%. Autologous fat injections were much more likely to cause CNS complications in association with ocular adverse events, making up 82.6% of the cases compared with 8.7% from HA injections. The variable particle size of autologous fat means that it can block various sized arteries including larger ones such as the ophthalmic artery.[18] This could lead to more diffuse downstream effects, which may explain why the ocular complications were more serious from autologous fat injection.

Prevention

It is important to have a keen understanding of prevention strategies to avoid blindness from filler,

© 2015 by the American Society for Dermatologic Surgery, Inc. Published by Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited.

be manufactured with thimerosal and should not be a compounded formula as this can increase allergenicity.[47] In the case of blindness, time is of the essence, making a skin test to evaluate for an allergic response impractical. An in vitro, dose–response study indicated that Juvederm (Allergan, Irvine, CA) is more resistant to hyaluronidase compared with Restylane (Galderma, Fort Worth, TX) perhaps because of the greater degree of cross-linking.[60] Therefore, higher doses of hyaluronidase may be needed with Juvederm products. The injector should consider injecting large volumes of hyaluronidase at the site of injection and surrounding areas if an HA filler was used. It has been shown that hyaluronidase can diffuse through the blood vessel walls without needing to be injected into the vessel directly.[58] Therefore, retrobulbar injection of hyaluronidase is a potential vision-saving treatment. To the best of the authors' knowledge, this strategy has not been attempted; however, they propose an injection of 300 to 600 units (2–4 mL) of hyaluronidase to the retrobulbar space. The technique involves placing a small amount of local anesthetic in the lower eyelid over the inferotemporal orbit. A 25-gauge needle is then advanced in that plane until it is at least 1 inch in depth. Then, 2 to 4 mL of hyaluronidase is injected into the inferolateral orbit.[47] One could also consider IV hyaluronidase or injection of the ophthalmic artery by a neuroradiologist with hyaluronidase.[47] However, these are hypothetical treatment strategies and have not been documented to date.

Other treatments that have been tried include mechanisms to decrease intraocular pressure including anterior chamber decompression, mannitol, and acetazolamide. Ocular massage may lower intraocular pressure and potentially increase blood flow or dislodge the embolus.[15] Retinal arterial dilation may be stimulated through carbon dioxide and oxygen inhalation. Hyperbaric oxygen has been recommended, but the concern with this is the time required to reach a location.[15] Systemic and local intra-arterial fibrinolysis has been attempted. This management strategy reflects studies showing improvement in central retinal artery occlusion secondary to thromboembolism when fibrinolysis was used.[61] However, fibrinolysis has not proven to be a successful treatment in the case of blindness from filler. Systemic corticosteroids to decrease the inflammatory component of the injury have also been recommended.

If any signs of cutaneous vascular compromise occur, it is important to treat that simultaneously. The authors previously reported on treatment strategies for vascular compromise in the skin, which included warm compresses, vigorous massage, and hyaluronidase if HA filler was used. Other treatments to consider include topical 2% nitroglycerin paste, aspirin, prednisone, and hyperbaric oxygen.[62]

The most important first step in the case of blindness is emergent assessment and management by an appropriate specialist. Injectors should know the ophthalmologists in their area to facilitate immediate transfer of the patient to that location. Whenever possible, the injecting physician or a staff member should accompany the patient to provide information about the filler used, location of injection, time of injection, and treatments instituted thus far. Furthermore, the injecting physician can review reported treatments and emphasize the timeline with the treating physician, as this may not be a complication he or she is familiar with. It is important to consider the possibility of CNS complications, and in such a scenario, the stroke service or a neurologist should be involved. Although many treatment strategies have been tried, none have definitive evidence. If any treatments are to be started, there is a 90-minute window to do this before the vision loss is permanent.[47]

Conclusion

With the increased use of soft tissue augmentation for revolumization, it is imperative to be aware of potential devastating ocular complications. Although the risk is very low, the authors believe that prevention begins with education and the ability to recognize potentially grave adverse events. Injectors should have a firm understanding of the vascular anatomy of high-risk sites and understand the depth and plane of injection. Key prevention strategies such as injecting small amounts under low pressure, using smaller needles or cannulas, and injecting slowly should be implemented. Despite proper technique, the possibility of embolization of filler into the ophthalmic artery

remains. As such, it is important that injectors have a management strategy in place, which should include immediate transfer to an ophthalmologist, and consideration of injection of high doses of hyaluronidase at the injection site and into the retrobulbar space in the case of HA filler. Further discussion among experts, relating their experiences with ocular complications from filler, is essential to build consensus that will improve patient safety and optimize outcomes.

References

1. FDA Safety Communication. Unintentional injection of soft tissue filler into blood vessels in the face. Available from: http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm448255.htm Accessed May 28, 2015.
2. Dreizen NG, Framm L. Sudden unilateral visual loss after autologous fat injection into the glabellar area. Am J Ophthal 1989;108:85–7.
3. Egido J, Arroyo R, Marcos A, Jimenez-Alfaro I. Middle cerebral artery embolism and unilateral visual loss after autologous fat injection into the glabellar area. Stroke 1993;24:615–6.
4. Teimourian B. Blindness following fat injections. Plast Reconstr Surg 1988;82:361.
5. Danesh-Meyer HV, Savino PJ, Sergott RC. Ocular and cerebral ischemia following facial injection of autologous fat. Arch Ophthalmol 2001;119:777–8.
6. Lee DH, Yang HN, Kim JC, Shyn KH. Sudden unilateral visual loss and brain infarction after autologous fat injection into the nasolabial groove. Br J Ophthalmol 1996;72:1026–7.
7. Chen Y, Wang W, Li J, Yu Y, et al. Fundus artery occlusion caused by cosmetic facial injection. Chin Med J 2014;127:1434–7.
8. Mori K, Ohta K, Nagano S. A case of ophthalmic artery obstruction following autologous fat injection in the glabellar area [in Japanese]. Nihon Ganka Gakkai Zasshi 2007;111:22–5.
9. Feinendegen DL, Baumgartner RW, Schroth G, Mattle HP, et al. Middle cerebral artery occlusion and ocular fat embolism after autologous fat injection in the face. J Neurol 1998;245:53–4.
10. Lee YJ, Kim HJ, Choi KD, Choi HY. MRI restricted diffusion in optic nerve infarction after autologous fat transplantation. J Neuroophthalmol 2010;30:216–8.
11. Feinendegen DL, Baumgartner RW, Vuadens P, Schroth G, et al. Autologous fat injection for soft tissue augmentation in the face: a safe procedure? Aesthetic Plast Surg 1998;22:163–7.
12. Park SJ, Woo SJ, Park KH, Hwang JM, et al. Partial recovery after intraarterial pharmacomechanical thrombolysis in ophthalmic artery occlusion following nasal autologous fat injection. J Vasc Interv Radiol 2011;22:251–4.
13. Coleman SR. Avoidance of arterial occlusion from injection of soft tissue fillers. Aesthet Surg J 2002;22:555–7.
14. Yoon SS, Chang DI, Chung KC. Acute fatal stroke immediately following autologous fat injection in to the face. Neurology 2003;51:1151–2.
15. Lazzeri D, Agostini T, Figus M, Nardi M, et al. Blindness following cosmetic injections of the face. Plast Reconstr Surg 2012;129:994–1012.
16. Park SH, Sun HJ, Choi KS. Sudden unilateral visual loss after autologous fat injection in to the nasolabial fold. Clin Ophthalmol 2008;2:679–83.
17. Carle MV, Roe R, Novack R, Boyer DS. Cosmetic facial fillers and severe vision loss. JAMA Ophthalmol 2014;132:637–9.
18. Park SW, Woo SJ, Park KH, Huh JW, et al. Iatrogenic retinal artery occlusion caused by cosmetic facial filler injections. Am J Ophthalmol 2012;154:653–62.
19. Lee CM, Hong IH, Park SP. Ophthalmic artery obstruction and cerebral infarction following periocular injection of autologous fat. Korean J Ophthalmol 2011;25:358–61.
20. Kim Lee, Kim EJ, Jahng GH, Chang DI. Magnetic resonance findings in two episodes of repeated cerebral fat embolisms in a patient with autologous fat injection into the face. J Korean Neurosurg Soc 2012;51:312–5.
21. Han SJ, Kim JS, Chung SR, Shim YS, et al. Cerebral and ocular fat embolism after autologous fat injection into the face: confirmed by magnetic resonance spectroscopy. J Korean Neurol Assoc 2003;24:399–401.
22. Paik DW, Jang IB, Kim JS, Lee JH, et al. A case of visual loss and ophthalmoplegia following injection of hyaluronic acid into the glabella [in Korean]. J Korean Ophthalmol Soc 2013;45:971–6. Available from: http://pdf.medrang.co.kr/paper/pdf/Kjo2/054/Kjo2054-06-21.pdf Accessed February 8, 2015.
23. Park KH, Kim YK, Woo SJ, Kang SW, et al. Iatrogenic occlusion of the ophthalmic artery after cosmetic facial filler injections. A National survey by the Korean Retina Society. JAMA Ophthalmol 2014;132:714–23.
24. Peter S, Mennel S. Retinal branch artery occlusion following injection of hyaluronic acid (Restylane). Clin Experiment Ophthalmol 2006;34:363–4.
25. Kim YJ, Kim SS, Song WK, Lee SY, et al. Ocular ischemia with hypotony after injection of hyaluronic acid gel. Ophthal Plast Reconstr Surg 2011;27:152–5.
26. Kim SN, Byun DS, Park JH, Han SW, et al. Panophthalmoplegia and vision loss after cosmetic nasal dorsum injection. J Clin Neurosci 2014;21:678–80.
27. Kim EG, Eom TK, Kang SJ. Severe visual loss and cerebral infarction after injection of hyaluronic acid gel. J Craniofac Surg 2014;25:684–6.
28. Kwon SG, Hong JW, Roh TS, Kim YS, et al. Ischemic oculomotor nerve palsy and skin necrosis caused by vascular embolization after hyaluronic acid filler injection: a case report. Ann Plast Surg 2013;71:333–4.
29. He MS, Sheu MM, Huang ZL, Tsai CH, et al. Sudden bilateral vision loss and brain infarction following cosmetic hyaluronic acid injection. JAMA Ophthalmol 2013;131:1234–5.
30. Castillo GD. Management of blindness in the practice of cosmetic surgery. Otolaryngol Head Neck Surg 1989;100:559–62.
31. Hanke WC. Adverse reactions to bovine collagen. In: Klein AW, ed. Soft tissue augmentation in clinical practice: procedures and techniques. New York: Marcel Dekker; 1998; p. 145.
32. Stegman SJ, Chu S, Armstrong RC. Adverse reactions to bovine collagen implant: clinical and histological features. J Dermatol Surg Oncol 1988;14:39–48.
33. Kwon DY, Park MH, Koh SB, Dhong ES, et al. Multiple arterial embolism after illicit intranasal injection of collagenous material. Dermatol Surg 2010;36:1196–9.
34. Brawley FE. Injury to the eyes after paraffin injection for saddle nose. The Ophthalmic Record 1906;15:115–6.
35. Silva MT, Curi AL. Blindness and total ophthalmoplegia after aesthetic polymethylmethacrylate injection: case report. Arq Neuropsiquiatr 2004;62:873–4.

36. Kubota T, Hirose H. Permanent loss of vision following cosmetic rhinoplastic surgery. Jpn J Ophthalmol 2005;49:535–6.

37. Shin H, Lemke BN, Stevens TS, Lim MJ. Posterior ciliary-artery occlusion after subcutaneous silicone-oil injection. Ann Ophthalmol 1988;20:342–3.

38. Roberts SA, Arthurs BP. Severe visual loss and orbital infarction following periorbital aesthetic poly-(L)- lactic acid (PLLA) injection. Ophthal Plast Reconstr Surg 2012;28:68–70.

39. Sung MS, Kim HG, Woo KI, Kim YD. Ocular ischemia and ischemic oculomotor nerve palsy after vascular embolism of injectable calcium hydroxylapatite filler. Ophthal Plast Reconstr Surg 2010; 26:289–91.

40. Kim YJ, Choi KS. Bilateral blindness after filler injection. Plast Reconstr Surg 2013;131:298–9.

41. Chen Y, Tsai Y, Chao A, Huang YS, et al. Visual field defect after facial rejuvenation with Botulinum toxin type A and polyacrylamide hydrogel injection. Plast Reconst Surg 2010;125:249–50.

42. Apte RS, Solomon SD, Gehlbach P. Acute choroidal infarction following subcutaneous injection of micronized dermal matrix in the forehead region. Retina 2003;23:552–4.

43. Ozturk CN, Li Y, Tung R, Parker L, et al. Complications following injection of soft tissue filler. Aesthet Surg J 2013;33:862–77.

44. Hwang YH, Hwang JH, Kim JS. Branch retinal artery occlusion after periocular dermal filler injection. Retin Cases Brief Rep 2008;2:338–41.

45. Dayan S, Arkins JP, Mathison CC. Management of impending necrosis associated with soft tissue filler injections. J Drugs Dermatol 2001;10: 1007–12.

46. Global Aesthetic Market Study XII. Aliso Viejo, CA: Medical Insight Inc; 2014;274.

47. Carruthers JD, Fagien S, Rohrich R, Weinkle S, et al. Blindness caused by cosmetic filler injection: a review of cause and therapy. Plast Reconst Surg 2014;134:1197–201.

48. McCleve DE, Goldstein JC. Blindness secondary to injections in the nose, mouth, and face: cause and prevention. Ear Nose Throat J 1994: 74;182–8.

49. Larrabee WF, Makielski KH, Henderson JL. Surgical anatomy of the face (2nd ed). Philadelphia: Lippincott Williams & Wilkins; 2004; pp. 97–101.

50. Flowers FP, Breza TS. Surgical anatomy of the head and neck. In: Bolognia JL, Jorizzo JL, Schaffer JV, editors. Dermatology (3rd ed). China: Elsevier; 2012; p. 2235–6.

51. Kleintjes WG. Forehead anatomy: arterial variations and venous link of the midline forehead flap. J Plast Reconstr Aesthet Surg 2007;60: 593–606.

52. Saban Y, Andretto Amodeo C, Bouaziz D, Polselli R, et al. Nasal arterial vasculature. Medical and surgical applications. Arch Facial Plast Surg 2012;14:429–36.

53. Kim YS, Choi DY, Gil YC, Hu KS, et al. The anatomical origin and course of the angular artery regarding its clinical implications. Dermatol Surg 2014;40:1070–6.

54. Lee JG, Yang HM, Choi YJ, Favero V, et al. Facial arterial depth and relationship with facial muscular layer. Plast Reconstr Surg 2015;135: 437–44.

55. Marur T, Tuna Y, Demirci S. Facial anatomy. Clin Dermatol 2014:32; 14–23.

56. Standring S. Gray's anatomy: the practical basis of clinical practice (14th ed). Spain: Elsevier; 2008:1204.

57. Jung W, Youn KH, Won SY, Park JT, et al. Clinical implications of the middle temporal vein with regard to temporal fossa augmentation. Dermatol Surg 2014;40:618–23.

58. DeLorenzi C. Complications of injectable fillers, part II. Aesthet Surg J 2013;34:584–600.

59. Yoshimura K, Coleman SR. Complications of fat grafting how they occur and how to find, avoid, and treat them. Clin Plast Surg 2015;42: 383–8.

60. Jones D, Tezel A, Borrell M. In vitro resistance to degradation of hyaluronic acid dermal fillers by ovine testicular hyaluronidase. Dermatol Surg 2010;36:804–9.

61. Chen CS, Lee AW. Management of acute central retinal artery occlusion. Nat Clin Pract Neurol 2008;4:376–83.

62. Beleznay K, Humphrey S, Carruthers J, Carruthers A. Vascular compromise from soft tissue augmentation: experience with 12 cases and recommendations for optimal outcomes. J Clin Aesthet Dermatol 2014;7:45–51.

Address correspondence and reprint requests to: Katie Beleznay, MD, FRCPC, FAAD, Carruthers and Humphrey Cosmetic Medicine, Suite 820-943 West Broadway, Vancouver, BC V5Z 4E1, Canada, or e-mail: kbeleznay@gmail.com

ATTACHMENT D

Update on Avoiding and Treating Blindness From Fillers: A Recent Review of the World Literature

Aesthetic Surgery Journal
2019, Vol 39(6) 662–674

DOI: 10.1093/asj/sjz053
www.aestheticsurgeryjournal.com
OXFORD UNIVERSITY PRESS

Katie Beleznay, MD, FRCPC; Jean D.A. Carruthers, MD, FRCSC, FRC (OPHTH); Shannon Humphrey, MD, FRCPC; Alastair Carruthers, MD, FRCPC; and Derek Jones, MD

Abstract

Background: Sudden loss of vision secondary to filler treatments is a rare but catastrophic complication.

Objectives: The aim of this study was to update the published cases of blindness after filler injection that have occurred since we published our review of 98 cases in 2015, and to discuss prevention and management strategies.

Methods: A literature review was performed to identify all cases of visual complications caused by filler injection identified between January 2015 and September 2018.

Results: Forty-eight new published cases of partial or complete vision loss after filler injection were identified. The sites that were highest risk were the nasal region (56.3%), glabella (27.1%), forehead (18.8%), and nasolabial fold (14.6%). Hyaluronic acid filler was the cause of this complication in 81.3% of cases. Vision loss, pain, ophthalmoplegia, and ptosis were the most common reported symptoms. Skin changes were seen in 43.8% of cases and central nervous system complications were seen in 18.8% of cases. Ten cases (20.8%) experienced complete recovery of vision, whereas 8 cases (16.7%) reported only partial recovery. Management strategies varied greatly and there were no treatments that were shown to be consistently successful.

Conclusions: Although the risk of blindness from fillers is rare, practitioners who inject filler should have a thorough knowledge of this complication including prevention and management strategies.

Level of Evidence: 5

Editorial Decision date: February 15, 2019; online publish-ahead-of-print February 21, 2019.

The number of filler treatments performed globally has steadily increased, and in the United States the number of treatments annually has grown by >300% from 2000 to 2017.[1] As these procedures grow in popularity, we are also seeing an increase in related adverse events. A 10-year retrospective review (2007–2017) of the US Food and Drug Administration (FDA) Manufacturer and User Facility Device Experience (MAUDE) database reported 47 cases of blindness and 42 cases of vision impairment caused by filler injection.[2] This database encompasses mandatory reports of adverse events from manufacturers and

Dr Beleznay is a Clinical Instructor, Dr Humphrey is a Clinical Assistant Professor, and Dr A. Carruthers is a Clinical Professor, Department of Dermatology, University of British Columbia, Vancouver, BC, Canada. Dr J. Carruthers is a Clinical Professor, Department of Ophthalmology, University of British Columbia, Vancouver, BC, Canada. Dr Jones is a dermatologist in private practice in Los Angeles, CA.

Corresponding Author:
Dr Katie Beleznay, Suite 820, 943 West Broadway, Vancouver, BC V5Z 4E1, Canada.
E-mail: kbeleznay@gmail.com; Twitter: @DrKatieBeleznay

voluntary reports from healthcare professionals and consumers. The records contain information about the outcome of the event and any interventions taken; however, there are limitations to the data as MAUDE is a passive surveillance database and can suffer from underreporting. In addition, some of the MAUDE data are incomplete, there are no strict criteria used to define clinical entities such as vision impairment, and in this database even consumers can file reports.[2] There may or may not be overlap between the cases reported in the MAUDE database and the cohort of published cases we report on herein. Nevertheless, it is likely that there are many other cases of visual complications from filler not captured in the MAUDE database or in our review of the world literature.

Three-dimensional filler treatments are performed by injecting filler into the subcutaneous preperiosteal space, which is the space through which the facial vasculature courses. Inadvertent canalization of the blood vessels that supply the facial tissues is especially concerning as many of these vessels anastomose with the ophthalmic artery and its branches which supply the retina. Animal studies suggest that the retina is only able to survive ~90 minutes without blood supply.[3] However, a more recent publication suggests time to retinal infarction in the case of complete central retinal artery occlusion may be shorter, of the order of 12 to 15 minutes.[4] Unless the block caused by the filler is promptly reversed, vision compromise may occur.

Our initial 2015 publication[5] on this devastating complication found 98 published cases of filler-related visual compromise in the world literature between 1906 and 2015. This follow-up paper describes a further 48 published cases from January 2015 through September 2018, bringing the total to 146 cases. Although the reported incidence is still small, the rate does appear to be increasing.

METHODS

The corresponding author (K.B.), with assistance from the College of Physicians and Surgeons of British Columbia librarian, conducted a Boolean search of the databases of the National Library of Medicine, Ovid MEDLINE, and Cochrane Library for the following string: (soft tissue augmentation OR filler OR injectable) AND (blindness OR ophthalmoplegia OR vision OR visual impairment OR retinal artery occlusion OR ophthalmic artery occlusion). The search was conducted in September 2018 and was limited to the English-language literature. In addition, the references cited in the identified articles were reviewed to identify any additional reports. The review was limited to injected fillers and associated ocular complications reported between January 2015 and September 2018.

RESULTS

A total of 48 new cases of filler-induced vision changes were identified between January 2015 and September 2018. Table 1 provides a description of the cases, the therapies employed, and the outcomes following therapy.

The most common locations of filler injection that caused vision changes were the nasal region (56.3%, n = 27), the glabella (27.1%, n = 13), the forehead (18.8%, n = 9), and the nasolabial fold (NLF) (14.6%, n = 7) (Figure 1). Of the 27 nasal injections, 12 were listed as nose, 7 nasal dorsum, 4 perinasal, 2 nasal bridge, 1 nasal tip, and 1 had injections in both the nasal tip and dorsum. Less common sites were the temple (2 cases), cheek (2 cases), chin (1 case), and upper eyelid (1 case). The exact anatomic location of injection was not listed in 1 case.

Hyaluronic acid (HA) was the filler that resulted in the greatest number of cases (81.3%, n = 39), followed by calcium hydroxylapatite (CaHa) (10.4%, n = 5). There was 1 case each (2.1%) from injections of autologous fat and polylactic acid (PLA). In 1 case the patient was told she had been injected with platelet-rich plasma (PRP), although the authors of that paper speculate that something else was injected in order to be viscous enough to occlude the arteries. The filler type was not reported (NR) in 1 case (Figure 2).

Geographically most cases were reported from Korea (n = 17), China (n = 8), Thailand (n = 6), the United States (n = 6), and Taiwan (n = 5). There was 1 case each out of Poland, Israel, Italy, Australia, Malaysia, and Japan (Figure 3).

Signs and Symptoms

On initial presentation, 26 cases (54.2%) were found to have complete unilateral vision loss, whereas the remaining cases had partial vision loss. In 27 cases (56.3%) pain was reported as 1 of the initial symptoms (described as periorbital, ocular, periocular, orbital, eye pain, or headache). In 21 cases (43.8%) associated skin changes, commonly described as erythematous to violaceous mottling or skin necrosis, were reported. Ophthalmoplegia (decreased extraocular movement) was reported in 26 cases (54.2%) and ptosis was seen in 25 cases (52.1%). Most commonly, the ophthalmoplegia and ptosis recovered completely. Nausea and/or vomiting were described as a presenting symptom in 8 cases (16.7%). Among the 48 cases, there were 9 cases (18.8%) of central nervous system (CNS) complications, including stroke-like features such as unilateral weakness or evidence of brain infarction on imaging. No deaths were reported. Ten cases (20.8%) reported complete recovery of vision, whereas 8 cases (16.7%) resulted in partial recovery of vision. Of the remaining cases, 25 (52%) had complete

Table 1. Cases of Visual Complications in the World Literature

Case	Type of filler	Injection site	Symptoms	Signs	Management	Outcome (variable time for follow-up)	Country
1	Autologous fat	Forehead	RE vision loss, ocular pain, flashes of light	RE NLP, RAPD right eye	Within 20 minutes: ocular massage and ocular drops (0.5% timolol, brimonidine, and dorzolamide) and IV dexamethasone, IV mannitol, 40% glycerol PO, 500 mg acetazolamide PO, IV aprostadil, subsequent vinpocetine PO daily	RE vision recovery (slow improvement occurred over 90 min)	Poland[28]
2	CaHa	Nasal bridge	LE blurred vision, diplopia, periorbital pain, headache, vomiting	LE vision 20/63, ophthalmoplegia, exotropia, skin changes nose, glabella, and forehead	Systemic steroids, antibiotics, hyperbaric oxygen therapy	LE vision and skin recovery, motility improved	Taiwan[29]
3	CaHa	Nasal tip and nasal dorsum	LE decreased vision, headache nausea, vomiting	LE hand motion 30 cm, ophthalmoplegia, dilated pupil, RAPD, skin necrosis nasal dorsum, glabella, left forehead	Alprostadil, dextran, hyperbaric oxygen therapy	LE vision improved to 6/60	Taiwan[30]
4	CaHa	Both temples, both cheeks, forehead, chin	Right periobital pain, diplopia, nausea, vomiting	20/25 vision RE, ptosis, ophthalmoplegia, hematoma at injection area right temple	Oral steroids	Vision NR, ptosis resolved, RE abduction deficit marginally improved	United States[31]
5	CaHa	Nasal bridge (previous rhinoplasty)	RE blurred vision, periocular pain	RE vision 20/20 3 hours post, 20/32 2 months post, ophthalmoplegia, ptosis, RE exotropia, bruising on the nose bridge, and forehead	Aspirin, hot water compresses, aspiration of material injected; enoxaparin, acetylsalicylic acid, amoxicillin/clavulanate, prednisone, topical antibiotics, eyedrops, and ointment	RE vision 20/60 18 months post, visual field deterioration, ptosis, and ophthalmoplegia resolved	Israel[32]
6	CaHa	Glabella	LE decreased vision, diplopia, nausea, impaired consciousness	LE 20/200, ophthalmoplegia, dilated pupil without reflex, conjunctival injection, purpura glabella to left forehead, unable to sit by herself	Systemic steroids	LE 20/25, fixed dilated pupil, resolved ophthalmoplegia, consciousness improved after 2 days, necrosis and scarring of glabella	Japan[33]
7	HA	Nasal dorsum	RE vision loss, eye pain 2 days after admission, "cold" sensation	RE vision NLP, ptosis, ophthalmoplegia, conjunctival injection, subconjunctival hemorrhage, fixed pupil, proptosis, increased intraocular pressure, pustular lesions on forehead and nose, subsequent necrosis	1 week after, 1200 U HYAL injected into orbital apex diluted in 15 mL, 600 U HYAL into skin, ocular massage, IV fluids, IV steroids, antibiotics,	RE vision NLP, ptosis, ophthalmoplegia improved, skin improvement	United States[34]
8	HA	Mid-face (cheek)	RE vision loss, RE pain, right ear pain, headache, dizziness, and subjective left-sided face and arm weakness	No lid ptosis or proptosis, no facial change or arm weakness on her left side	Arrived for treatment within 20 minutes, 150 U HYAL into infraorbital foramen, 150 U into supraorbital notch, retrobulbar injection of 450 U of HYAL, 325 mg of aspirin	RE vision recovery	United States[6]
9	HA	Nose (27G cannula)	LE decreased vision, LE pain, nausea	LE light perception, ptosis, ophthalmoplegia, purple discoloration over left orbital area, forehead, nasal bridge, MRI acute infarction	6 hours later: 450 mL HYAL into nasal area, hyperbaric oxygen, low-level laser therapy, anterior chamber paracentesis, methylprednisolone, antiplatelet drugs, oral antibiotic given plus antiepileptic drug to prevent seizures, topical steroid and antibiotic eye drops	2 months later: LE vision light perception only; lid ptosis and ophthalmoplegia resolved, microphthalmia	Thailand[10]

Table 1. Continued

Case	Type of filler	Injection site	Symptoms	Signs	Management	Outcome (variable time for follow-up)	Country
10	HA	Nose (27G cannula)	RE vision loss, pain	RE vision NLP, ptosis, ophthalmoplegia, RAPD	450 mL HYAL nasal area, self-ocular massage (10 seconds for 3 cycles every hour for 24 hours), breathing into plastic bag, carbogen for 30 minutes every 2 hours, hyperbaric oxygen 5 hours after, oral acetazolamide, eye drop of dorzolamide + timolol, 325 mg PO aspirin daily	RE vision loss, recovery of ophthalmoplegia and ptosis	Thailand[10]
11	HA	Nose (25G cannula)	RE blurry vision, periorbital pain, HA	RE visual field defect, erythematous patch on nose and glabella area	15 min: 300 U HYAL to nose, nitroglycerin transdermal pad on chest; self ocular massage for 6 hours, rebreathing into a plastic bag; subsequent pulse electromagnetic frequency; hyperbaric oxygen 4 hours post	Recovery of visual field defect	Thailand[10]
12	HA	Nose (cannula)	RE vision loss, RE periorbital pain, HA, nausea, vomiting	RE vision NLP, pupil not reactive to light, ophthalmoplegia, ptosis, skin discoloration nasal tip and surrounding area	2 mL HYAL into nasal area, subsequent repeat nasal HYAL, next day 1000 U HYAL retrobulbar (which helped pain, EOM movement, ptosis), IV parecoxib, metoclopramide, acetazolamide, carbogen, timolol drops, and aspirin; subsequent hyperbaric oxygen	Vision NR, resolved ophthalmoplegia and ptosis	Thailand[10]
13	HA	Forehead (25G cannula)	LE decreased vision, headache	LE vision light perception only, ptosis, ophthalmoplegia, pupil dilated and slow reaction to light, purple discoloration along left supraorbital and supratrochlear arteries and upper eyelid, small subacute infarction left temporal lobe	Within 15 minutes: 9 mL intralesional HYAL and 8 mL retrobulbar HYAL (150 U/mL), nitroglycerin pad applied to chest, ocular massage, rebreathing in a plastic bag; IV antibiotic, systemic steroid and hyperbaric oxygen therapy; pulsed electromagnetic frequency applied	LE vision light perception only, ptosis partially improved, ophthalmoplegia almost fully improved	Thailand[10]
14	HA	Left temple (23G needle)	LE blurred vision (after second 0.1 mL deep on bone)	Blurred vision (visual exam NR) LE ptosis	7.5 mL HYAL (600 U/mL) injected over left forehead and temporal area; 2.5 mL HYAL (600 U/mL) then injected into and around supratrochlear notch; ocular massage for >4.5 hours and 90 minutes of hyperbaric oxygen performed	LE vision recovery; vision began to improve after injection into supratrochlear notch	Thailand[10]
15	HA	Glabella and nasal dorsum	RE vision loss inferior half of field, RE periorbital pain, HA	RE counting fingers, ophthalmoplegia, exotropia, erythematous skin discoloration over glabella, dorsum, and tip of the nose	HYAL 60 IU/mL subcutaneously over glabella and nasal dorsum 12 hours after start of symptoms	RE vision recovery, recovery of ophthalmoplegia and visual field defect, minimal skin scarring	Malaysia[35]
16	HA	Nasal tip	RE blurred vision, pain, dizziness	Decreased vision (visual exam NR), ptosis, ophthalmoplegia, chemosis and injection RE, erythematous patches on periocular and glabella region progression to necrosis	1500 U HYAL injected around injection site, methylprednisolone, nitroglycerin, alprostadil, prophylactic antibiotics, and daily dressing plus low-level laser therapy	No visual field defects, ophthalmoplegia, ptosis, skin all recovered	Korea[36]

Table 1. Continued

Case	Type of filler	Injection site	Symptoms	Signs	Management	Outcome (variable time for follow-up)	Country
17	HA	Glabella and nasal dorsum (needle)	Vision loss	Type 1 (n = 2): no ptosis, no ophthalmoplegia Type 2 (n = 2): ptosis, no ophthalmoplegia; Type 3 (n = 2): no ptosis, ophthalmoplegia; Type IV (n = 3): ptosis, ophthalmoplegia (all 4 types showed vision loss)	NR	Type 1 (n = 2): no ptosis, ophthalmoplegia, enophthalmos; Type 2 (n = 2): ptosis improved, mild enophthalmos; Type 3 (n = 2): ophthalmoplegia improved, mild enophthalmos; Type 4 (n = 3): ophthalmoplegia, ptosis recovered (except 1 patient with strabismus), enophthalmos present, no improvement in vision	Korea[37]
18	HA	Glabella and nasal dorsum (needle)	Vision loss		NR		Korea[37]
19	HA	Glabella (needle)	Vision loss		NR		Korea[37]
20	HA	Glabella (needle)	Vision loss		NR		Korea[37]
21	HA	Glabella (needle)	Vision loss		NR		Korea[37]
22	HA	NLF (needle)	Vision loss		NR		Korea[37]
23	HA	NLF (needle)	Vision loss		NR		Korea[37]
24	HA	NLF (needle)	Vision loss		NR		Korea[37]
25	HA	Nasal dorsum (needle)	Vision loss		NR		Korea[37]
26	HA	Glabella, perinasal area, NLF	Vision loss, ocular pain	Vision NLP for 3 cases, 1 case hand motion, ophthalmoplegia (all 4 patients), skin necrosis (2 patients)	One patient had intra-arterial thrombolysis	Vision loss NLP all 4 patients, ophthalmoplegia improved in 3 of 4 cases, ocular misalignment	Korea[38]
27	HA	Glabella, perinasal area, NLF					Korea[38]
28	HA	Glabella, perinasal area, NLF				.	Korea[38]
29	HA	Glabella, perinasal area, NLF					Korea[38]
30	HA	Nose	LE decreased vision, orbital pain, HA, dizziness, nausea, vomiting	LE ptosis, ophthalmoplegia conjunctival injection, LE dilated pupil, color change forehead, nasal tip, medial side of orbit	HYAL (location not described), systemic steroid injections, antibiotics; skin lesion dressed with epidermal growth factor spray and antibacterial ointment	Vision NR, diplopia progressively resolved, skin improved with barely any scarring	Korea[39]
31	HA (29G needle)	Upper eyelid (superior sulcus)	RE blurred vision, pain, swelling and heaviness of RE	RE vision 20/400, slit lamp showed filler material in right anterior chamber	Temporal limb incision RE and irrigation and aspiration to remove filler (10 days post injection); gatifloxacin and rimexolone eye drops	RE vision 20/20; no residual filler in anterior chamber	Korea[40]
32	HA	Glabella	LE decreased vision	LE vision hand motion, ophthalmoplegia, ptosis, increased intraocular pressure, multiple cerebral infarctions, muscle weakness, dysarthria	NR	Vision NLP, ophthalmoplegia and weakness improved	Korea[41]
33	HA	Nose	LE vision loss after 1 hour	LE NLP, ptosis	Retrobulbar HYAL, 1500 U × 2 (300 U/mL solution) (32 hours later), partial RA recanalization	NLP	China[8]

Table 1. Continued

Case	Type of filler	Injection site	Symptoms	Signs	Management	Outcome (variable time for follow-up)	Country
34	HA	Nose	RE reduced vision	RE hand motion 5 cm, ptosis, ophthalmoplegia, visual field defect	Retrobulbar HYAL 1500 U × 1 (12 hourrs later), corticosteroids, no recanalization	20/60	China[8]
35	HA	Nose	LE vision loss	LE NLP, ptosis	Retrobulbar HYAL 3000 U × 2 (34 hours later), corticosteroids, partial recanalization	NLP	China[8]
36	HA	Forehead	LE reduced vision	LE 20/200, ptosis, ophthalmoplegia, visual field defect	Retrobulbar HYAL 1500 U × 2 (4 hours later), corticosteroids	NLP	China[8]
37	HA	Forehead (23G blunt cannula)	RE vision loss, ocular pain	RE NLP, ptosis, purple discoloration over nose, forehead	1500 U HYAL to forehead, nose, glabella, retrobulbar (>7 hours later), hyperbaric oxygen, aspirin, oral acetazolamide, IV dexamethasone	RE vision hand movements, skin improved	China[7]
38	HA	Nasal dorsum	RE pain, diplopia	20/20 initial then 20/200, ptosis, ophthalmoplegia, strabismus, exotropia, pupil dilation, visual field defect, erythematous to violaceous discoloration nasal dorsum and glabella	Topical timolol, tobramycin-dexamethasone ophthalmic eye drops, ocular massage, IV prostaglandin E1, periocular injection of anisodamine, IV dextran, IV ozagrel, oxygen therapy, IM methylcobalamin, dexamethasone, topical antibacterial	Vision improved to 20/16, ocular position normalized, skin healed normally	China[42]
39	HA	NR	RE vision loss, pain	RE NLP	HYAL subcutaneous, hyperbaric oxygen, oral acetazolamide, IV injections Ginkgo biloba extract, cobamamide, dexamethasone	NLP	China[43]
40	HA	Forehead	RE vision loss	RE NLP, pupil fixed, dilated, nonreactive, mottled erythema around injection site	HYAL injection (no details), ocular massage, hyperbaric oxygen therapy	RE vision loss, skin improved (decreased erythema)	China[44]
41	HA	Nose	RE vision loss, left upper limb weakness 9 hours later	RE vision loss, weakness left elbow, left hand and wrist	NR	RE vision loss, persistent upper-limb weakness	Taiwan[45]
42	HA	Nose	RE vision loss, ocular pain, nausea, dizziness	RE ptosis, no light reflex, ecchymosis over nasal and glabellar area, left upper-limb weakness, brain infarcts on MRI	NR	NR	Taiwan[46]
43	HA	Glabella and nasal dorsum (needle)	RE vision loss	RE vision loss	IATT was performed using 1000 U HYAL and 60,000 U urokinase into the trunk of the right ophthalmic artery	RE vision loss	Taiwan[47]
44	HA	Brow	RE decreased vision, flashing sensation	Vision NR initial, subsequent MRI ophthalmic review normal	HYAL brow and forehead (375 IU/mL) then 300 U (0.8 mL) HYAL twice in area of supratrochlear and supraorbital notches (relief after second injection)	Vision recovery	Australia[9]
45	HA (patient told this by injector)	Forehead, nose	Vision NR, pain	LE ptosis, eyelid edema, subconjunctival hemorrhage, necrosis skin forehead, glabella, nasal skin, no loss of visual function	Oral antibiotic therapy and topical warm packs; subsequent IV antibiotics, IV methylprednisolone plus daily application of collagenase-antibiotic ointment	Vision recovery, LE ptosis recovered, 1 month after, some skin scarring	Italy[48]
46	NR	Nose	LE decreased vision	LE vision finger counting, best corrected 20/200	NR	20/100	United States[49]

Table 1. Continued

Case	Type of filler	Injection site	Symptoms	Signs	Management	Outcome (variable time for follow-up)	Country
47	Patient told injection was PRP, but not viscous so likely something else	Forehead	RE vision loss, RE pain, syncope	RE vision loss, ptosis, left-sided hemiparesis, forehead necrosis	Antibiotic ointment for skin and pulsed dye laser to the scar	RE vision loss, residual weakness of left upper and lower extremity	United States[50]
48	Polylactic acid	Forehead	RE vision decreased, RE pain, dizziness, left upper and lower extremity weakness and loss of consciousness	RE counting fingers progressed to NLP, RE RAPD, skin necrosis right forehead, neurologic exam unremarkable	IV methylprednisolone and 60 mg prednisone	RE vision loss, skin lesions improved	United States[51]

CaHa, calcium hydroxylapatite; HYAL, hyaluronidase; IV, intravenous; LE, left eye; NLP, no light perception; NR, not reported; PO, per os (by mouth); PRP, platelet-rich plasma; RAPD, relative afferent pupillary defect; RE, right eye; U, units. • Note that only English-language articles were included in this review. There was 1 paper in which the abstract was available in English that reported 18 cases out of a single institution between 2014 and 2016. This paper was not included in the analysis. For 6 patients the injection site was the forehead, 8 patients were injected in the nose, and the other 4 patients were injected in both sites. The injected material was autologous fat and HA. Only 3 patients showed improvement of vision, the rest remained with no light perception.[52] • There was another case of blindness reported in the Netherlands of blindness after HA injection into the nasal dorsum. Only the abstract was available in English and so it was not included in this review.[53] • There was 1 case reported from the US FDA MAUDE database where compensation was given to the plaintiff after HA filler injected into the temple caused permanent blindness; however, given the limited details and uncertainty as to whether this had been published previously and in what year the case occurred, it was not included.[2]

vision loss, 1 had worsened vision, vision remained the same in 2 cases, and the outcome was not reported in 2 cases. Treatments were employed in all cases where there was vision recovery, and are discussed in more detail below. It is important to note that in only 1 of the 10 cases of complete vision recovery was there documentation of no light perception prior to intervention. In the other 9 cases that described full recovery of vision there was either no reported initial objective visual exam, the vision was reduced and documented as counting fingers or with visual acuities ranging from 20/400 to 20/63, or a visual field defect was described.

Treatments included ocular massage, intraocular pressure–lowering agents, intravenous (IV) steroids, subcutaneous and retrobulbar hyaluronidase (RBH), and IV thrombolytic therapies. Given the lack of consistent reporting on treatment, and the wide variety of treatments, it is hard to draw conclusions regarding efficacy. In 13 of 48 cases (27%) the treatments used were not reported. Commonly reported treatments include the use of hyaluronidase in 51% (20/39 cases where HA filler was used), systemic steroids in 35.4% (17/48 total cases), and hyperbaric oxygen in 20.8% (10/48). In 1 case of complete and 2 cases of partial vision recovery, RBH was used;[6–8] however, only 1 case of complete recovery was attributed directly to the RBH.[6] One case that improved from no light perception to hand movement received multiple treatments, including RBH, instituted 7 hours after injection.[7] Another case had RBH injected 12 hours after filler treatment; this patient's vision improved from hand motion at 5 cm to 20/60, but the authors commented that the treatment likely made no contribution to this partial recovery of vision, because it coincided with the resolution of corneal edema and the gradual absorption of retinal hemorrhage.[8] In 2 cases of complete vision recovery hyaluronidase was injected in the region of the supraorbital or supratrochlear notch and it was reported to immediately bring resolution to the visual disturbance.[9,10]

DISCUSSION

Background

With the increased use of soft tissue fillers, it is important to be aware of potential devastating ocular complications. To minimize the risk of intravascular injection, injectors should have a thorough knowledge of vascular anatomy and a complete understanding of risk factors and safe injection techniques. Further, they should be able to recognize the symptoms and signs of vascular compromise and be able to implement a treatment protocol immediately should this complication occur. The potential for vision loss, skin necrosis, and CNS complications such as stroke should be included on consent forms. Although this complication is very rare, informed consent requires that the practitioner review this potential life-altering condition with the patient.

A clear understanding of vascular anatomy can minimize the risks of complications. The ophthalmic artery begins behind the eye, branching into vessels including the supraorbital, supratrochlear, and dorsal nasal arteries (Figure 4). When high-risk sites such as the glabella, nose,

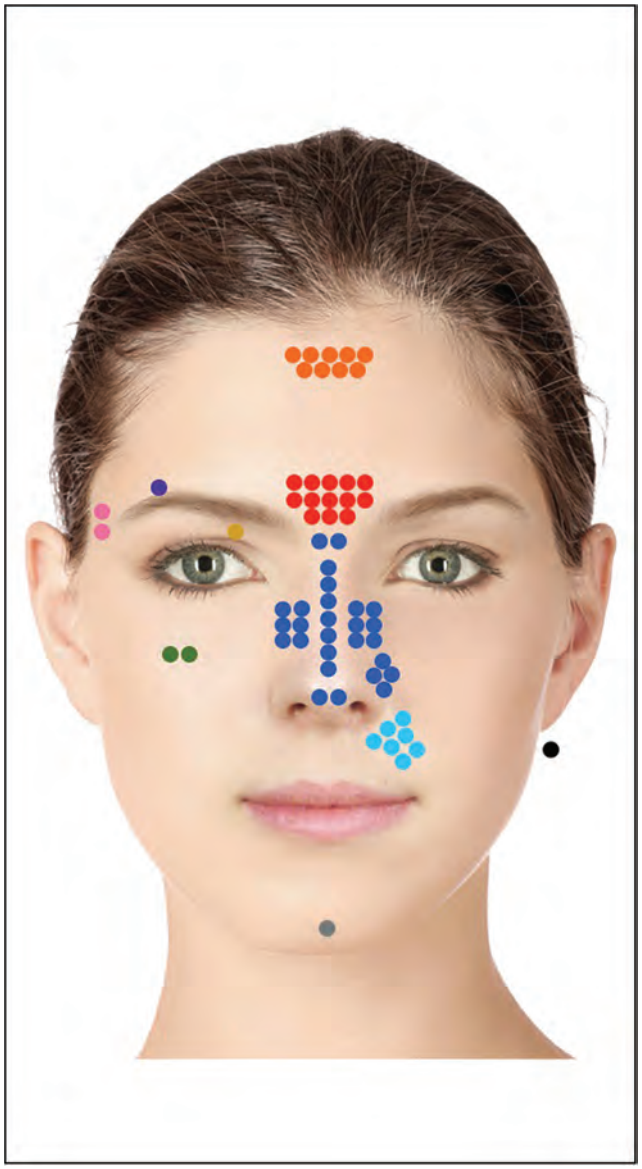


Figure 1. Location of filler injection resulting in visual complication. The single black dot represents a case where the anatomic location of injection was not specified.

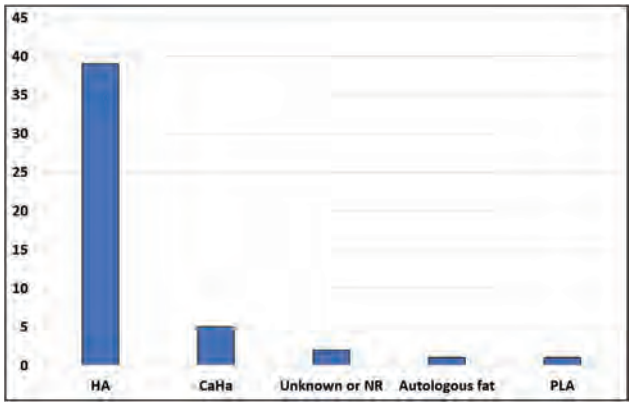


Figure 2. Number of cases of visual complications from each filler type.

Figure 3. Geographic distribution of cases of visual complications from filler.

and forehead are injected, there is a risk of intra-arterial injection of filler. However, there are many anastomoses between different arteries of the face and branches of the ophthalmic artery system, putting virtually any anatomic location of injection at risk for ocular complications.[5] It should also be stated that expert mastery of vascular anatomy is not failsafe as vascular anatomy is highly variable and vascular events may still occur in the hands of experienced and expert injectors.[11]

Vascular complications can occur when injecting with a needle or a cannula. Detailed documentation of the needle or cannula type used was only reported in 16 of 48 cases (33.3%). A needle was used in 10 cases and cannula in 6 cases, with the cannula size ranging from 27G to 23G. Cannulas have been shown to cause vascular complications in other studies, and in 1 survey 17% of injectors who noted vascular complications were injecting fillers with cannulas, most commonly 25G, but also 23G.[11]

The mechanism of action of blindness after filler injection has been hypothesized to involve intra-arterial injection of filler followed by subsequent retrograde embolization into the ophthalmic artery system (Figure 4).[12] When enough filler is delivered into a vessel and pushed retrogradely with injection pressures greater than the sum of the systolic arterial pressure and the frictional forces due to viscous flow, embolization to the ophthalmic artery can

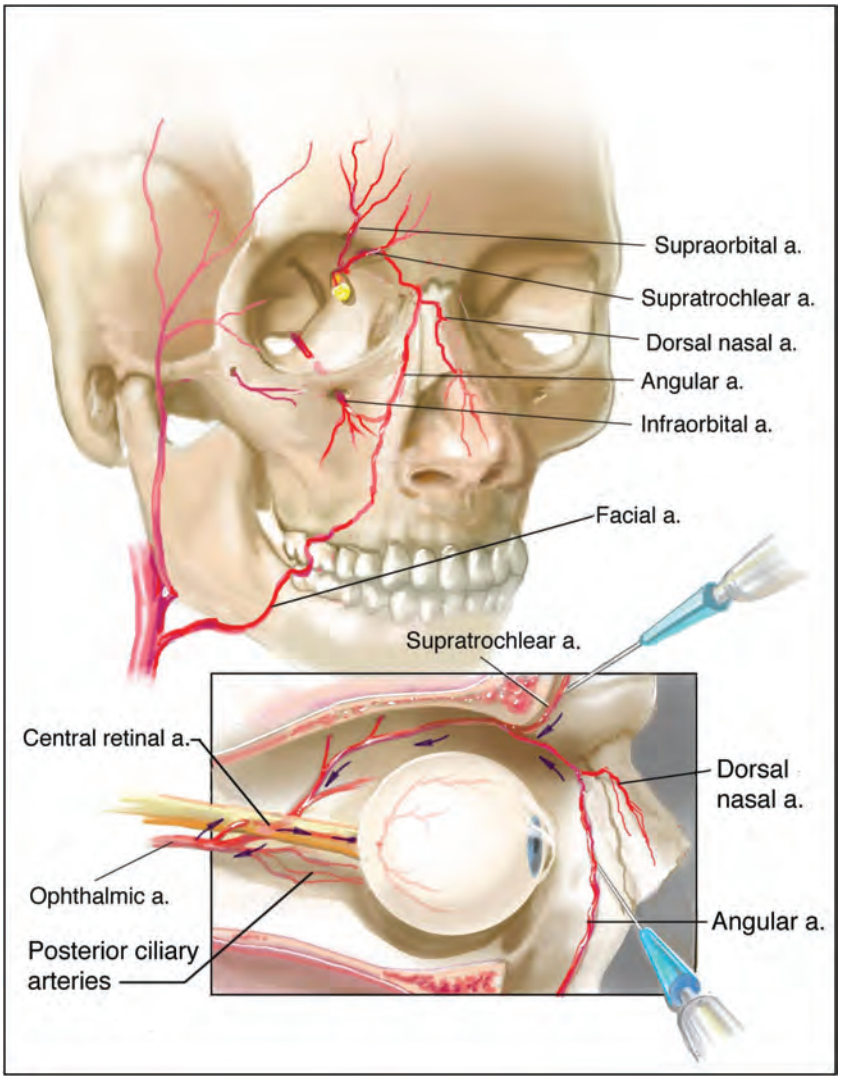


Figure 4. Vascular anatomy of the face. A selection of facial vessels are highlighted here. This is one depiction of the blood vessels of the face and there is individual anatomic variability. Inset demonstrates the mechanism of action of filler-induced blindness. In this diagram, filler is shown being injected directly into the supratrochlear artery or into the angular artery, which anastomoses with the supratrochlear artery. From here filler can travel retrogradely, as shown by the arrows, into the ophthalmic artery and its branches, blocking blood supply to the retina and causing visual complications.

occur.[13] In a recent cadaver head perfusion model, injection pressures above the systolic arterial pressure were needed to transfer filler into the ophthalmic artery (166.7 mm Hg).[12] Furthermore, it does not take a large volume to occlude the vessel. In 1 study the average volume of filler necessary to fill the supratrochlear artery from the glabella to the bifurcation of the ophthalmic and central retinal arteries was 0.085 mL (range, 0.04–0.12 mL).[14] Filler can be dispersed to multiple vessels with enough pressure and travel retrogradely to the orbit or to the internal carotid artery and cerebral circulation, causing CNS complications, and/or distally to the smaller branches supplying the skin. This is consistent with the clinical finding in this report of skin and CNS complications occurring in 43.8% and 18.8%, respectively, of the cases of visual compromise after filler injection.

Clinical Features

This update shows that HA filler causes 81.3% of cases of visual complications compared to 2.1% due to autologous fat. This is in contrast to our last paper[5] where autologous fat was the leading cause (47.9%) of complications. The increase in cases involving HA filler is likely caused by the growing popularity of HA as a filling agent in recent years because of its reversibility and favourable safety profile. According to ASPS data, HA fillers made up 77.7% of the soft-tissue filler market in the United States in 2017.[1]

This update showed 10 cases (20.8%) with complete recovery of vision and 8 cases (16.7%) with partial recovery of vision. Previously[5] there were only 2 cases out of 98 (2%) with complete vision recovery. This improvement

in outcome from this complication could reflect the fact that more cases were reported with HA filler, which has been shown to offer better outcomes than autologous fat.[5] It is also possible that general preparedness, education, and early intervention may be responsible for the improved outcomes. This remains to be substantiated by a larger dataset.

Thirty-eight cases (79.2%) were reported in Asia. There are limited data to evaluate why the great majority of cases were found in this region. This preponderance could represent a reporting bias: many of the large case series have come from Asia. Further, "diamond-shaped reflation" to increase the anterior projection of the central face has become culturally desirable in Asia.[15] This area includes the glabella, nose, medial cheek, and NLF, sites that are high-risk anatomic locations for injections.

This update showed that the nose has surpassed the glabella as the most common location for this complication at 56.3% of cases followed by the glabella (27.1%), forehead (18.8%), and NLF (14.6%) (Figure 1). In our previous publication, the highest-risk location was the glabella (38.8%), nasal region (25.5%), NLF (13.3%), and forehead (12.2%).[5]

Visual compromise most commonly occurred immediately after injection. Ocular pain or headache occurred in the majority of cases (56.3%). Nausea and vomiting secondary to increased intraocular pressure occurred in 8.2% of cases. Obstruction of the blood supply to the extraocular muscles or innervating nerves caused ophthalmoplegia in 54.2% of cases. Reduced blood supply to the levator palpebrae superioris muscle or its innervating nerves caused ptosis in 52.1% of cases. Although vision recovery was less common due to the permanence of retinal damage, ophthalmoplegia and ptosis more commonly recovered, likely because the nerves and muscle regenerate after vascular compromise. Skin changes, including necrosis and subsequent scarring, were seen in 43.8% of cases. Central nervous system complications, including stroke-like features, were seen in 18.8% of cases.

Prevention

Because there is an absence of documented, validated, effective treatments for blindness arising from filler injections, the most rational strategy for avoiding blindness from fillers is prevention. Although evidence is lacking, numerous strategies have been proposed to avoid adverse events such as vision loss. The following are the key prevention strategies:

1) Be familiar with the anatomy, location, and depth of facial vessels and the common variations. Injectors should understand the optimal depth and plane of injections at different sites. The safest plane to be injecting is likely deep and directly on bone or very superficially in the dermis. The subcutaneous plane, although frequently injected to achieve cosmetic improvement, is the highest-risk location as the vasculature most commonly courses through this region.
2) Inject slowly and with minimal pressure.
3) Consider using a cannula. Some authors recommend a cannula in the belief it is less likely to pierce blood vessels. However, there are cases of vascular compromise from cannulas of various sizes. A consensus paper on this topic recommended that for those who use cannulas, a 25G or larger is preferred as a 27G or smaller cannula has a greater potential to penetrate arterial walls.[16]
4) Inject small increments at a time to prevent a bolus of filler traveling retrogradely.
5) Move the needle tip while injecting to avoid depositing a large amount of filler in one location.
6) Aspirate before injection. This recommendation is controversial because it may not be possible to retrieve flashback into a syringe through fine needles when thick gels are involved. Additionally, the small size and collapsibility of facial vessels restrict the efficacy of aspiration.[17]
7) Exercise extreme caution when injecting a patient who has undergone a previous surgical procedure in the area.
8) Consider mixing the filler with epinephrine to promote vasoconstriction because it is more difficult to cannulate a vasoconstricted artery.
9) Consider using targeted digital pressure to occlude major periorbital vessels and prevent inadvertent retrograde travel of filler.[18] A cadaveric study[19] showed that compressing the superior nasal corners with the fingers during cosmetic filler injections reduced the risk of filler traveling into the orbit. This technique may be particularly beneficial when injecting high-risk areas such as the nose.

Treatment

Prior to instituting a treatment strategy, it is important to document the vision changes and confirm the diagnosis, providing this assessment does not significantly delay treatment. Whenever possible, immediate evaluation by an ophthalmologist is best. Some of the cases reported were criticized for not having recorded any objective measurements as there is the possibility that vascular visual spastic events may mimic vascular embolic events (such as classic or retinal migraine).[20] Near vision should be checked (33 cm) with a visual acuity chart, with 1 eye being checked at a time. If this chart is unavailable, getting the patient to read a magazine or count fingers will suffice. The swinging flashlight test can be performed to screen for normal pupillary reaction. Extraocular movements and ptosis should be evaluated and fundoscopy should

also be considered. The patient should be asked about any pain, visual changes, weakness in the extremities, or other symptoms such as nausea, headache, and dizziness. A strength exam of the extremities should be performed. Skin findings, including any blanching, erythema, duskiness, or reticulate changes, should be documented and capillary refill tested in the affected area.

Many injectors do not have experience with treating ocular complications although they may be aware of the reported issues. When possible, practitioners injecting cosmetic fillers should have an established working relationship with their ophthalmologic colleagues who have been previously briefed about this rare but potentially devastating emergency and who understand the importance of timely help. In addition, those who are injecting HA filler should have a sufficient and routinely updated supply of hyaluronidase immediately available in case this should be required. These 2 steps allow the patient to be seen and treated without the potential delay that can easily occur in a busy emergency department. If there is any concern about CNS involvement the stroke team or a neurologist should be involved.

Currently there is no evidence-based, accepted standard of care for treating visual compromise caused by filler. Treatments that have been employed vary widely and successful strategies are rare. Treatment should be instituted urgently before the damage secondary to retinal ischemia is irreversible.[3,4] If an HA filler was used, hyaluronidase should be injected into the skin at the site of injection and along the path of anastomosing arteries. Physicians could also consider injecting hyaluronidase into the area of the supraorbital or supratrochlear notch in an attempt to cannulate the arteries and push the hyaluronidase retrogradely. Cannulating these arteries is likely to prove very challenging; however, there have been 2 reported cases of immediate recovery of vision with this technique.[9,10] The application of hyaluronidase via a retrobulbar or peribulbar injection has been described[21,22] as a method of getting hyaluronidase closer to the area of blockage. It is controversial whether this technique is successful at salvaging vision loss and what sort of practitioners should be attempting this technique. There have been several anecdotal successes with RBH in this context.[23] In this update 3 cases experienced partial or complete vision recovery after treatment with RBH although only 1 case[6] directly attributed success to the RBH. However, RBH did not improve vision in other reports.[8,24] Controversy over the efficacy of RBH continues; we have at this stage more hypothesis than evidence. Other treatments that can be instituted in the office include topical timolol,[25,26] rebreathing into a paper bag,[16,26] ocular massage,[16,25,26] and oral aspirin.[16,25,26] Treatments that may be considered by an ophthalmologist or appropriate specialist include intravenous acetazolamide,[16,25,26] mannitol,[25,26] prostaglandins,[26] anterior chamber paracentesis,[16,25,26] sublingual glyceryl trinitrate,[16] hyperbaric oxygen,[25,26] or direct intravascular or IV injection of hyaluronidase with urokinase.[16,27] Heparin, systemic steroids, and antibiotics could also be considered.[25,26]

Limitations

The primary limitation is that this is a retrospective review of case reports. Case reports are inherently limited, because the quality of the conclusions we can extract is limited by the data that are reported. Inconsistent details were included in each case report and in many cases details were sparse. One particular challenge is identifying the specific anatomic sites that cause blindness as in some cases more than 1 injection location was listed. As such, all locations where injections were performed at the time of visual compromise were documented and for the sake of completeness we have included them all herein. So, for example, in one case the temples, cheeks, forehead, and chin were all injected and the authors did not specify or know which site caused the visual compromise. For the purposes of Figure 1 each location was listed as a potential location for visual compromise; however, it is unlikely that the chin injection was the cause of blindness as it is less high risk than the other injection sites. Although we have tried to identify and review all the cases of visual complications from filler that have been published in the English world literature, this may likely underrepresent the true number of cases due to unreported cases or those documented in the non-English literature.

CONCLUSIONS

There were 48 cases of blindness following filler treatment reported in the world literature between January 2015 and September 2018. During the same time period approximately 9.5 million cosmetic filler procedures were performed in the United States alone.[1] Although visual complications are inevitably underreported in the literature as reflected by the higher numbers seen in the US FDA's MAUDE database,[2] the risk of blindness remains extremely low. Nevertheless, 48 newly published cases in nearly 4 years is an increase over 98 cases published from 1906 to 2015, bringing the total number of cases to 146 in 113 years. This increase in incidence could be the result of the growing number of filler treatments being performed (including an increase in nonexpert injectors) as well as an increase in reporting.

For the years 2015 to 2018, the majority (81.3%) of published cases of vision compromise caused by filler were from HA filler; and the highest-risk injection location was the nose (56.3% of cases). Our previous report of 98 cases of

visual compromise caused by filler between 1906 and 2015 showed that autologous fat was the most common cause. The increased reports of complications from HA fillers could reflect the rise in popularity of this filler type in recent years.

With the increasing global popularity of filler injections, it is important that injectors are aware of the risks of blindness from filler and are prepared to do everything they can to mitigate that risk. Our goal with this paper was to collate the reports in the medical literature, highlight some of the clinical features, and report the treatment strategies that have been employed in order to stimulate discussion. Further research with animal or human cadaveric models to evaluate treatments and other novel approaches would help to expand our understanding of this complication. Currently, the visual prognosis is most often grave and the majority of cases have proved irreversible. No universal consensus exists with regards to the best treatment strategies; however, injectors should be aware of management strategies, be prepared to implement them urgently, and/or elicit the assistance of colleagues who can help manage this complication. We must continue to learn from the experience of others, share our knowledge, and communicate openly to build consensus in order to reduce the risk of this devastating complication and improve outcomes.

Acknowledgments

The authors would like to acknowledge Louise Gagnon for editorial support.

Disclosures

The authors declared no potential conflicts of interest with respect to the research, authorship, and publication of this article.

Funding

The authors received no financial support for the research, authorship, and publication of this article.

REFERENCES

1. American Society of Plastic Surgeons. 2017 Plastic Surgery Statistics Report. https://plasticsurgery.org/documents/News/Statistics/2017/cosmetic-procedure-trends-2017.pdf. Accessed December 1, 2018.
2. Rayess HM, Svider PF, Hanba C, et al. A Cross-sectional analysis of adverse events and litigation for injectable fillers. *JAMA Facial Plast Surg.* 2018;20(3):207-214.
3. Hayreh SS, Podhajsky PA, Zimmerman B. Nonarteritic anterior ischemic optic neuropathy: time of onset of visual loss. *Am J Ophthalmol.* 1997;124(5):641-647.
4. Tobalem S, Schutz JS, Chronopoulos A. Central retinal artery occlusion - rethinking retinal survival time. *BMC Ophthalmol.* 2018;18(1):101.
5. Beleznay K, Carruthers JD, Humphrey S, Jones D. Avoiding and treating blindness from fillers: a review of the world literature. *Dermatol Surg.* 2015;41(10):1097-1117.
6. Chestnut C. Restoration of visual loss with retrobulbar hyaluronidase injection after hyaluronic acid filler. *Dermatol Surg.* 2018;44(3):435-437.
7. Hu XZ, Hu JY, Wu PS, Yu SB, Kikkawa DO, Lu W. Posterior ciliary artery occlusion caused by hyaluronic acid injections into the forehead: a case report. *Medicine (Baltimore).* 2016;95(11):e3124.
8. Zhu GZ, Sun ZS, Liao WX, et al. Efficacy of retrobulbar hyaluronidase injection for vision loss resulting from hyaluronic acid filler embolization. *Aesthet Surg J.* 2017;38(1):12-22.
9. Goodman GJ, Clague MD. A rethink on hyaluronidase injection, intraarterial injection, and blindness: is there another option for treatment of retinal artery embolism caused by intraarterial injection of hyaluronic acid? *Dermatol Surg.* 2016;42(4):547-549.
10. Thanasarnaksorn W, Cotofana S, Rudolph C, Kraisak P, Chanasumon N, Suwanchinda A. Severe vision loss caused by cosmetic filler augmentation: case series with review of cause and therapy. *J Cosmet Dermatol.* 2018;17(5):712-718.
11. Goodman GJ, Roberts S, Callan P. Experience and management of intravascular injection with facial fillers: results of a multinational survey of experienced injectors. *Aesthetic Plast Surg.* 2016;40(4):549-555.
12. Cho KH, Dalla Pozza E, Toth G, Bassiri Gharb B, Zins JE. Pathophysiology study of filler-induced blindness. *Aesthet Surg J.* 2019;39(1):96-106.
13. Lazzeri D, Spinelli G, Zhang YX, Nardi M, Lazzeri S. Panophthalmoplegia and vision loss after cosmetic nasal dorsum injection. *J Clin Neurosci.* 2014;21(5):890.
14. Khan TT, Colon-Acevedo B, Mettu P, DeLorenzi C, Woodward JA. An anatomical analysis of the supratrochlear artery: considerations in facial filler injections and preventing vision loss. *Aesthet Surg J.* 2017;37(2):203-208.
15. Bae JM, Lee DW. Three-dimensional remodeling of young Asian women's faces using 20-mg/ml smooth, highly cohesive, viscous hyaluronic acid fillers: a retrospective study of 320 patients. *Dermatol Surg.* 2013;39(9):1370-1375.
16. Humzah MD, Ataullah S, Chiang C, Malhotra R, Goldberg R. The treatment of hyaluronic acid aesthetic interventional induced visual loss (AIIVL): a consensus on practical guidance. *J Cosmet Dermatol.* 2019;18(1):71-76.
17. Carey W, Weinkle S. Retraction of the plunger on a syringe of hyaluronic acid before injection: are we safe? *Dermatol Surg.* 2015;41(Suppl 1):S340-S346.
18. Rodriguez LM, Martin SJ, Lask G. Targeted digital pressure to potentially minimize intravascular retrograde filler injections. *Dermatol Surg.* 2017;43(2):309-312.
19. Tansatit T, Moon HJ, Apinuntrum P, Phetudom T. Verification of embolic channel causing blindness following filler injection. *Aesthetic Plast Surg.* 2015;39(1):154-161.
20. Fagien S. Commentary on a rethink on hyaluronidase injection, intra-arterial injection and blindness. *Dermatol Surg.* 2016;42(4):549-552.
21. Carruthers JD, Fagien S, Rohrich RJ, Weinkle S, Carruthers A. Blindness caused by cosmetic filler

injection: a review of cause and therapy. *Plast Reconstr Surg.* 2014;134(6):1197-1201.
22. Carruthers J, Fagien S, Dolman P. Retro or peribulbar injection techniques to reverse visual loss after filler injections. *Dermatol Surg.* 2015;41(Suppl 1):S354-S357.
23. DeLorenzi C. Commentary on: efficacy of retrobulbar hyaluronidase injection for vision loss resulting from hyaluronic acid filler embolization. *Aesthet Surg J.* 2017;38(1):23-27.
24. Hwang CJ, Mustak H, Gupta AA, Ramos RM, Goldberg RA, Duckwiler GR. Role of retrobulbar hyaluronidase in filler-associated blindness: evaluation of fundus perfusion and electroretinogram readings in an animal model. *Ophthalmic Plast Reconstr Surg.* 2019;35(1):33-37.
25. de Lacerda D. Prevention and management of iatrogenic blindness associated with aesthetical filler injections. *Dermatol Ther.* 2018;31(6):e12722.
26. Walker L, King M. Visual loss secondary to cosmetic filler injection aesthetic complications. *J Clin Aesthet Dermatol.* 2018;11(5):E53-E55.
27. Chiang C, Zhou S, Chen C, Ho DS, Zhang H, Liu K. intravenous hyaluronidase with urokinase as treatment for rabbit retinal artery hyaluronic acid embolism. *Plast Reconstr Surg.* 2016;138(6):1221-1229.
28. Szantyr A, Orski M, Marchewka I, Szuta M, Orska M, Zapała J. Ocular complications following autologous fat injections into facial area: case report of a recovery from visual loss after ophthalmic artery occlusion and a review of the literature. *Aesthetic Plast Surg.* 2017;41(3):580-584.
29. Sung WI, Tsai S, Chen LJ. Ocular complications following cosmetic filler injection. *JAMA Ophthalmol.* 2018;136(5):e180716.
30. Chou CC, Chen HH, Tsai YY, Li YL, Lin HJ. Choroid vascular occlusion and ischemic optic neuropathy after facial calcium hydroxyapatite injection—a case report. *BMC Surg.* 2015;15:21.
31. Dagi Glass LR, Choi CJ, Lee NG. Orbital complication following calcium hydroxylapatite filler injection. *Ophthalmic Plast Reconstr Surg.* 2017;33(3S Suppl 1):S16-S17.
32. Cohen E, Yatziv Y, Leibovitch I, et al. A case report of ophthalmic artery emboli secondary to calcium hydroxylapatite filler injection for nose augmentation—long-term outcome. *BMC Ophthalmol.* 2016;16:98.
33. Marumo Y, Hiraoka M, Hashimoto M, Ohguro H. Visual impairment by multiple vascular embolization with hydroxyapatite particles. *Orbit.* 2018;37(3):165-170.
34. Ramesh S, Fiaschetti D, Goldberg RA. Orbital and ocular ischemic syndrome with blindness after facial filler injection. *Ophthalmic Plast Reconstr Surg.* 2018;34(4):e108-e110.
35. Sharudin SN, Ismail MF, Mohamad NF, Vasudevan SK. Complete recovery of filler-induced visual loss following subcutaneous hyaluronidase injection. *Neuro-Ophthalmol.* 2018. doi: 10.1080/01658107.2018.1482358.
36. Bae IH, Kim MS, Choi H, Na CH, Shin BS. Ischemic oculomotor nerve palsy due to hyaluronic acid filler injection. *J Cosmet Dermatol.* 2018;17(6):1016-1018.
37. Myung Y, Yim S, Jeong JH, et al. The classification and prognosis of periocular complications related to blindness following cosmetic filler injection. *Plast Reconstr Surg.* 2017;140(1):61-64.
38. Kim A, Kim SH, Kim HJ, Yang HK, Hwang JM, Kim JS. Ophthalmoplegia as a complication of cosmetic facial filler injection. *Acta Ophthalmol.* 2016;94(5):e377-e379.
39. Lee JI, Kang SJ, Sun H. Skin necrosis with oculomotor nerve palsy due to a hyaluronic acid filler injection. *Arch Plast Surg.* 2017;44(4):340-343.
40. Kim DY, Eom JS, Kim JY. Temporary blindness after an anterior chamber cosmetic filler injection. *Aesthetic Plast Surg.* 2015;39(3):428-430.
41. Lee WS, Yoon WT, Choi YJ, Park SP. Multiple cerebral infarctions with neurological symptoms and ophthalmic artery occlusion after filler injection. *J Korean Ophthalmol.* 2015;56(2):285-290.
42. Chen W, Wu L, Jian Xl, et al. Retinal branch artery embolization following hyaluronic acid injection: a case report. *Aesthet Surg J.* 2016;36(7):NP219-NP224.
43. Shi H, Liang LL, Cui ZH. Ophthalmic artery occlusion after cosmetic facial filler injections. *JAMA Ophthalmol.* 2018;136(6):e180764.
44. Hao JL, Pant OP, Lu CW. Central retinal artery occlusion following hyaluronic acid fillers injection. *Am J Med Sci.* 2018;356(2):e25.
45. Li KT, Huang YH, Chen CH, Chou LW. Delayed-onset cerebral infarction after cosmetic facial injection using hyaluronic acid. *J Formos Med Assoc.* 2016;115(7):587-588.
46. Lin YC, Chen WC, Liao WC, Hsia TC. Central retinal artery occlusion and brain infarctions after nasal filler injection. *QJM.* 2015;108(9):731-732.
47. Chen YC, Wu HM, Chen SJ, et al. Intra-arterial thrombolytic therapy is not a therapeutic option for filler-related central retinal artery occlusion. *Facial Plast Surg.* 2018;34(3):325-329.
48. Salval A, Ciancio F, Margara A, Bonomi S. Impending facial skin necrosis and ocular involvement after dermal filler injection: a case report. *Aesthetic Plast Surg.* 2017;41(5):1198-1201.
49. Shahlaee A, Sridhar J, Rahimy E, Shieh WS, Ho AC. Paracentral acute middle maculopathy associated with postviral Purtscher-like retinopathy. *Retin Cases Brief Rep.* 2019;13(1):50-53.
50. Prado G, Rodríguez-Feliz J. Ocular pain and impending blindness during facial cosmetic injections: is your office prepared? *Aesthetic Plast Surg.* 2017;41(1):199-203.
51. Ragam A, Agemy SA, Dave SB, Khorsandi AS, Banik R. Ipsilateral ophthalmic and cerebral infarctions after cosmetic polylactic acid injection into the forehead. *J Neuroophthalmol.* 2017;37(1):77-80.
52. Hu XZ, Chen SQ, Zhang Q, Wu PS, Lu W. Clinical analysis of visual loss caused by facial cosmetic fillers injection. *Zhonghua Yan Ke Za Zhi.* 2017;53(8):594-598.
53. Schelke LW, Fick M, van Rijn LJ, Decates T, Velthuis PJ, Niessen F. [Unilateral blindness following a non-surgical rhinoplasty with filler]. *Ned Tijdschr Geneeskd.* 2017;161:D1246.

www.nature.com/scientificreports

scientific reports

Check for updates

OPEN

Disastrous cerebral and ocular vascular complications after cosmetic facial filler injections: a retrospective case series study

Fanfan Zhao[1], Yao Chen[2], Dong He[1], Xiangxi You[3] & Yuyun Xu[1]✉

Soft tissue filler injections are among the most popular facial rejuvenation methods. Cerebral infarction and ophthalmic artery occlusion are rare and catastrophic complications, especially when facial cosmetic fillers are injected by inexperienced doctors. Radiologists and plastic surgeons need to increase their awareness of the complications associated with fillers, which allows early diagnosis and intervention to improve patient prognosis. Regarding the mechanism by which vascular occlusion occurs after facial filler injections, a retrograde embolic mechanism is currently the predominant theory. Numerous case reports have been presented regarding complications associated with injections of facial aesthetics. However, the small sample sizes of these studies did not allow for an adequate assessment of the clinical and imaging manifestations based on the location of the occlusion and the type of filler, and detailed elaboration of multiple cerebral infarctions is also lacking. Therefore, this study aimed to investigate the clinical and radiological features of severe cerebral and ocular complications caused by cosmetic facial filler injections. In addition, we discuss the pathogenesis, treatment, and prognosis of these patients. The clinical, computed tomography (CT), magnetic resonance imaging (MRI), and digital subtraction angiography (DSA) findings were described and analysed. Radiological examinations are crucial for demonstrating severe complications, and brain MRI is especially strongly suggested for patients with cosmetic filler-induced vision loss to identify asymptomatic cerebral infarctions. Extreme caution and care should be taken during facial injections by plastic surgeons.

Soft tissue filler injections are among the most popular nonsurgical facial rejuvenation methods worldwide; more than 5.5 million filler injections were used in 2014, and more than $11 billion in revenue was generated annually[1,2]. Among these fillers, hyaluronic acid (HA) is a frequently used injectable filler, and more than 800,000 Americans receive HA injections each year due to its durability, biocompatibility, reabsorption, and cost effectiveness[3]. Despite the high safety profile of HA, complications can occur, especially when HA is injected by inexperienced doctors or via substandard "syringes"[4].

Cerebral infarction and ophthalmic artery occlusion are rare but catastrophic complications of cosmetic filler injections[5]; they occur mainly after filler injection into the glabellar and nasal regions, the nasolabial fold, or the forehead, in order of reported cases, with a rather low overall incidence[6]. The mechanism of retinal artery occlusion after facial cosmetic filler injection is proposed to be retrograde embolization. The backflow of substances from the injection area into the internal carotid artery and small facial arteries occurs due to pressure and the vascular network, leading to complications such as ocular and cerebral infarction, skin ischaemia and necrosis[7] (Fig. 1). Patients typically present with sudden vision loss, headache, altered consciousness, and limb weakness

[1]Center for Rehabilitation Medicine, Department of Radiology, Zhejiang Provincial People's Hospital (Affiliated People's Hospital), Hangzhou Medical College, Hangzhou, Zhejiang, China. [2]Department of Radiology, 903 Hospital of the Joint Service Support Force of the Chinese People's Liberation Army, Hangzhou, Zhejiang, China. [3]Department of Radiology, The First People's Hospital of Jiashan, Jiaxing, Zhejiang, China. ✉email: xuyuyun@hmc.edu.cn

ATTACHMENT D

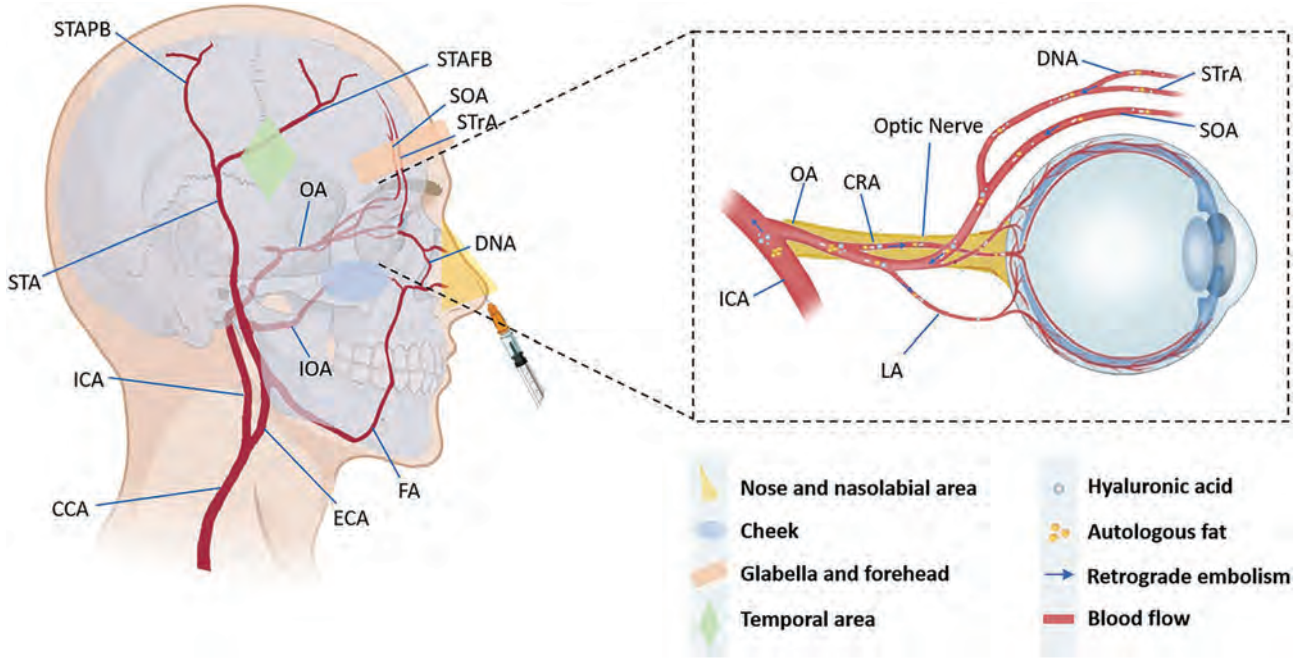


Figure 1. Schematic drawing of the facial region vascular anatomy and the possible obstruction mechanism of hyaluronic acid and autologous fat injection. The illustration shows that the substances in the injection region flowed back into the internal carotid artery and small facial arteries due to pressure and the vascular network, resulting in complications such as ocular and cerebral infarction, skin ischaemia and necrosis. CCA, Common carotid artery; ICA, internal carotid artery; ECA, external carotid artery; IOA, infraorbital artery; FA, facial artery; STA, superficial temporal artery; STrA, supra-trochlear artery; SOA, supraorbital artery; STAFB, superficial temporal artery frontal branch; STAPB, superficial temporal artery parietal branch; DNA, dorsal nasal artery; OA, ophthalmic artery; CRA, central retinal artery; LA, lacrimal artery.

during or shortly after the filling procedure. Rapid and extensive cerebral ischaemia and postinfarction haemorrhage can lead to irreversible brain damage and even death[4].

Therefore, awareness of serious filler-related complications is crucial, as patient outcomes could be improved with early diagnosis and appropriate interventions[8]. Attempts towards determining the radiological manifestations of complications resulting from HA filler injection have already been reported. Kim et al.[9] proposed cerebral angiographic features of ophthalmic and retinal artery obstruction associated with cosmetic facial fillers in seven patients undergoing intra-arterial thrombolytic therapy (IATT). However, due to the small sample size, clinical and imaging features could not be adequately assessed on the basis of the location of the occlusion or the type of filler. Park et al.[10] conducted a nationwide survey to describe the clinical and angiographic features of 44 Korean cases with medically induced occlusion of the ophthalmic artery and its branches due to cosmetic facial filler injections. This study generally presents the imaging manifestations of complications following facial filler injections and classifies occlusions of the ophthalmic artery and its branches into 6 types according to fluorescein angiographic findings. However, one limitation of this approach is the lack of detailed descriptions of cerebral infarctions caused by these injections.

This study aimed to investigate the clinical and radiologic features of iatrogenic occlusion of the cervical-cerebral artery and its branches caused by cosmetic facial filler injections. In addition, we discuss the pathogenesis, treatment, and prognosis of these patients and briefly review the related literature.

Methods

Study sample

The Ethics Committee of Zhejiang Provincial People's Hospital (ZJPPH) review board approved this retrospective study and waived the requirement for written informed consent. To protect patient privacy, all the data were desensitized before use, and relevant prescribed guidelines were implemented in this study.

Between January 2017 and August 2023, a total of 193 patients with a clinical diagnosis of "retinal artery occlusion" or "ophthalmic artery occlusion" were collected from the ZJPPH. Some patients were excluded from this study to ensure that the complete radiological manifestations were observed. The exclusion criteria were as follows: patients with duplicate names (n = 5), patients without a history of cosmetic facial filler injections (n = 169), and patients without radiological examination (n = 7). Finally, twelve patients were included in this study (Fig. 2).

We reviewed all the patient demographics, clinical characteristics, and imaging manifestations from the electronic medical records, including the injection filler material, injection site, injection dose, time interval between the injection and symptoms, initial and final visual acuity, initial symptoms and signs, diagnosis, treatment,

ATTACHMENT D

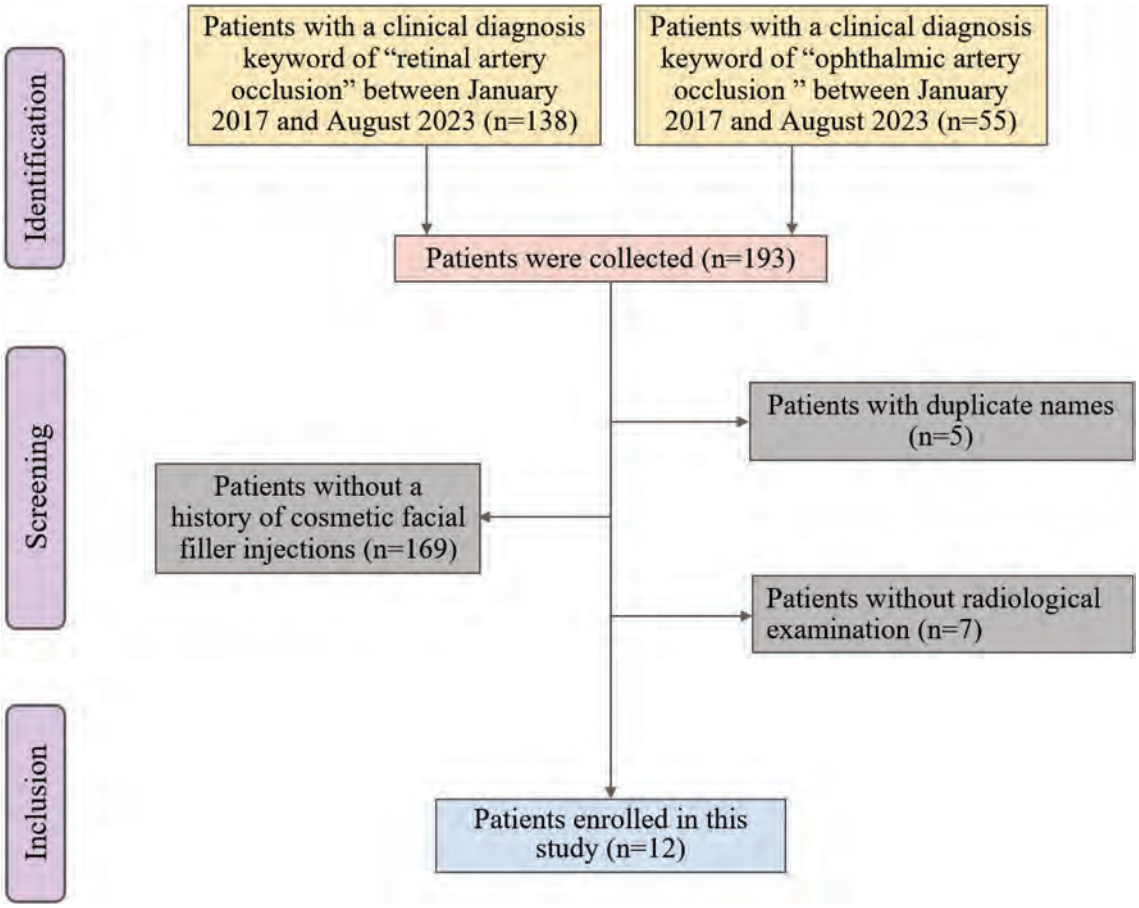


Figure 2. Flow diagram of the process used to select subjects for this study.

hyaluronidase quantity, brain computed tomography (CT), magnetic resonance imaging (MRI), and digital subtraction angiography (DSA)[11].

The cases of iatrogenic retinal artery occlusion were classified on the basis of the presumed location obtained from fundus photographs and angiographic findings as follows[10]: (1) ophthalmic artery occlusion (OAO), (2) central retinal artery occlusion (CRAO), (3) branch retinal artery occlusion (BRAO), (4) supraorbital artery (SOA), and (5) ischaemic optic neuropathy (ION).

Imaging acquisition

CT: Unenhanced head CT scans were performed at a 5-mm slice thickness for six patients. The following scanner settings were used: 100–120 kVp, 512 × 512 matrix, and automatic tube current. CT angiogram (CTA) and CT perfusion (CTP) on an Aquilion One system (Toshiba Medical Systems, Otawara, Japan). Intravenous injection of 50 mL of Iohexol containing 350 mg of iodine per mL (Ominipaque, GE Healthcare, China) was administered at an injection rate of 3–4 mL/s. CT perfusion images were subsequently transmitted to the postprocessing platform to obtain cerebral blood volume (CBV), cerebral blood flow (CBF), mean transit time (MTT), time to peak (TTP), and delay time images.

MRI: Clinical routine MR images were obtained with a 3.0 T MRI scanner (Discovery MR 750, GE Healthcare) with an eight-channel head coil using the same MR parameters for all patients, including axial T1-weighted imaging (T1WI), T2-weighted imaging (T2WI), diffusion-weighted imaging (DWI), and T2-weighted fluid-attenuated inversion recovery (T2-FLAIR) images. All the sequences were performed with a section thickness = 5.5 mm and an interslice gap = 1.5 mm. Susceptibility-weighted imaging (SWI) was performed for only one patient to investigate intracranial haemorrhage.

DSA: Cerebral DSA was performed on a Philips Medical Systems machine at six fps and 75 kVp. Superselective intra-arterial thrombolysis with hyaluronidase was attempted for four patients after providing informed consent. The patients were placed in the supine position, and after routine local disinfection, a 6F catheter sheath was placed on the C1 level using the Seldinger technique. Then, the microcatheter was introduced along with the guidewire, the tip of the microcatheter was placed at the proximal beginning of the ophthalmic artery, and 1500 U or 1200 U hyaluronidase (in combination with 10 ml of saline) was slowly injected[12].

Analysis of radiological data

All radiological data were analysed by two neuroradiologists (F.Z. and Y.C., with 5 and 8 years of work experience, respectively) who independently reviewed the images. Any discrepancy between the two doctors was

ATTACHMENT D

resolved by consulting with a third board-certified radiologist (Y.X., with 17 years of head and neck radiology work experience). The imaging findings of the lesions, such as the location, size, CT density, signal intensity on MRI, cerebral artery morphology on CTA, and perfusion changes on CTP, were reviewed.

Results

Study population

Twelve patients (10 patients who received HA injections and 2 patients who received autologous fat injections) with ophthalmic or retinal artery obstruction associated with facial cosmetic filler injections were analysed in this study. A total of twelve women were included, and the mean age was 38.5 ± 11.3 years (range, 22–61 years). The amount of HA filler injected was 0.1–0.3 ml. The mean time from onset to hospitalization was 19.4 h (range 0.5–72 h), and the mean follow-up period was 25.7 ± 21.3 days (range, 7–90 days).

Clinical characteristics

The nose area was the most common site at which HA was injected (50%, 5/10), and caused occlusion of the artery (2 patients with OAO, 2 patients with CRAO, 1 patient with BRAO, and 2 patients with ACI). The second most common site was the glabellar region (n = 3, 1 patient with OAO, 1 patient with CRAO, 1 patient with BRAO and SOA), followed by the preorbital region (n = 1, 1 patient with CRAO and ACI) and the cheek area (n = 1, 1 patient with CRAO and ACI). However, the injection of autologous fat entirely into the cheek (100%, 2/2) resulted in CRAO and OAO, respectively. A total of 66.7% (8/12) of patients did not receive IATT after the embolism occurred but were treated with a retrobulbar injection of hyaluronidase (RIH), anterior chamber paracentesis (ACP), or massage at the hospital. A total of 33.3% (4/12) of patients who were provided with an IATT showed improvement in visual acuity. The visual prognosis was poor, with 5 patients (41.7%) having a final visual acuity of no light perception (NLP). The demographic and clinical characteristics are presented in Table 1.

Case No	Sex/age (y)	Eye	Diagnosis	Cosmetic Injection			Symptom to hospital (h)	Initial symptoms	Treatments	Hyaluronidase	Visual acuity		Follow-up (day)
				Material	Site	Dose (ml)					Initial	Final	
1	F/46	R	CRAO, ACI	HA	Preorbital	0.1	4	SLOV	IATT	1500U	NLP	LP	7
2	F/31	R	OAO, ACI	HA	Nose	–	5	SLOV, headache and left limb paralysis	RIH	–	NLP	NLP	14
3	F/31	L	CRAO, ACI	HA	Nose	0.2	4.5	SLOV, headache, nausea and vomiting,	IATT	1500U	NLP	0.2	24
4	F/31	R	OAO	HA	Glabella	0.3	0.5	SLOV, ocular pain, headache, ptosis	IATT	1500U	NLP	LP	15
5	F/61	R	OAO	HA	Nose	0.2	20	SLOV, ophthalmo-plegia	RIH	1500U	0.2	0.3	90
6	F/22	R	CRAO, ACI	HA	Cheek	0.1	8	SLOV, headache	ACP	–	NLP	NLP	16
7	F/38	R	CRAO	HA	Glabella	0.1	4	Visual acu-ity decrease	RIH	300U	CF	CF	26
8	F/52	R	BRAO	HA	Nose	0.1	48	Visual acu-ity decrease, ocular pain	IATT	1200U	NLP	LP	23
9	F/43	R	OAO	Fat	Cheek	–	10	SLOV, ocu-lar pain	Massage	–	NLP	NLP	18
10	F/27	L	CRAO	HA	Nose	0.1	72	SLOV, headache, nausea and vomiting	RIH	1000U	NLP	NLP	30
11	F/35	R	BRAO, SOA	HA	Glabella	0.2	9	SLOV, headache, ocular pain, ptosis	RIH	1000U	NLP	CF	29
12	F/46	R	CRAO	Fat	Cheek	–	48	SLOV	ACP	–	NLP	NLP	16

Table 1. Demographic and clinical data of the patients. ACI: Acute cerebral infarction; CRAO: central retinal artery occlusion; OAO: ophthalmic artery occlusion; BRAO: branch retinal artery occlusion; SOA: supraorbital artery; HA: hyaluronic acid; SLOV: sudden loss of vision; IATT: intra-arterial thrombolytic therapy; RIH: retrobulbar injection of hyaluronidase; ACP: anterior chamber paracentesis; CF: counting fingers; LP: light perception; NLP: no light perception.

ATTACHMENT D

Radiologic findings

The main imaging findings of the patients are summarized in Table 2. In this study, eight patients underwent MR imaging of the brain, and the results showed abnormalities. Six patients also had corresponding neurologic symptoms, including headache (5 patients), contralateral hemiplegia (2 patients), and urinary incontinence (2 patients). DSA was performed in only 4 patients.

CT images: All eight noncontrast head CT scans from six patients obtained between 1 and 18 h after onset were negative. CTA of Patient 2 (Fig. 3) showed occlusion of the right ophthalmic artery and a normal left ophthalmic artery, while the CT perfusion image of the same patient showed that the perfusion parameters (CBF, CBV, MTT, and delay time) of the brain were normal.

MRI characteristics: Five of the 12 patients (41.7%) who underwent brain MR imaging exhibited multifocal acute/subacute infarction, representing 62.5% of all patients with a brain lesion and three unilateral and two bilateral cerebral hemispheres, mostly involving the frontal and parietal lobes, especially the watershed zones. The size of the lesions ranged from 3 mm to 7.5 cm in the greatest dimension. All lesions showed hypointense to isointense signals on T1WI and hyperintense to isointense signals on T2WI. Intracerebral haemorrhage was observed on SWI in Patient 2, as shown in Fig. 3, and when the patient's symptoms worsened, she was transferred to another hospital. Subarachnoid haemorrhage (SAH) was observed on FLAIR in Patient 6. Acute ischaemia of the right optic nerve manifested in Patients 2 and 6, with a swollen optic nerve and diffusion restriction on DWI (Figs. 3 and 4).

Catheter angiography: DSA was performed for four patients who received a superselective ophthalmic intra-arterial injection of 1200 U or 1500 U hyaluronidase. Blood flow to the eyeball was compromised, as flow stagnation in the distal branches of the ophthalmic artery was observed in all patients. Patient 1 exhibited right central retinal artery occlusion (Fig. 5) with a small infarction in the right frontal and occipital lobes. A filling defect in the left MCA was observed in Patient 3 (Fig. 6) with multiple cerebral infarction foci.

Treatment and outcome

The mean hospitalization duration was 6.8 days (range 3–11 days). Four patients received selective ophthalmic intra-arterial administration of hyaluronidase, five patients received retrobulbar hyaluronidase injections, two patients received anterior chamber paracentesis, and one patient received eye massage therapy. Five patients still had no light perception, while two showed significant improvement in visual acuity. Patient 2, who had severe cerebral infarction and postinfarction haemorrhage, was transferred to another hospital. The acute thrombosis lesion of the left MCA in Patient 3 was treated with stent extraction to ensure revascularization. Patients 1, 6 and 10 suffered from acute cerebral infarction and were treated with conservative hyperbaric oxygen therapy (HBOT).

Case No	Neurological symptoms and signs	CT/CTA	MRI	Cerebral infarction	DSA
1	None	Not available	ACI in right frontal and occipital lobes	Multifocal	Right CRAO
2	Headache and left limb paralysis, fatigue,	Head CT of 5 h after onset is normal. CTA of 7.5 h after onset shows right OAO	ACI in bilateral frontal, right parietal, and occipital lobes; Right ION SWI shows haemorrhage lesion two days later	Multifocal	Not performed
3	Headache, and right limb paralysis, urinary incontinence	Head CT scan after 3 h, 10 h, and 18 h of shows normal	ACI in left frontal and parietal lobes, left head of caudate nucleus	Multifocal	Left CRAO, left MCA thromboses
4	Headache, ptosis, nausea and vomiting	Head CT scan after 1 h shows normal	Not available	Not available	Right OAO
5	Headache, Nausea and vomiting, ophthalmoplegia	Not available	Not available	Not available	Right OAO
6	None	CTA of 8 h after onset shows OAO	ACI in bilateral frontal and parietal, left basal ganglia, right occipital lobes SAH; Right ION	Multifocal	Not performed
7	None	Head CT scan after 4 h shows normal	Right ION	Not available	Not performed
8	None	Head CT scan after 2 h shows normal	Not available	Not available	Not performed
9	None	CTA of 7.5 h after onset shows right OAO	Right ION	Not available	Not performed
10	Urinary incontinence	Not available	ACI with haemorrhage in the left frontoparietal lobes, Left ION	Multifocal	Not performed
11	Headache, ptosis	Head CT scan shows normal	Not available	Not available	Not performed
12	None	Not available	Right ION	Not available	Not performed

Table 2. Radiological manifestations of the patients. ACI: Acute cerebral infarction; OAO: ophthalmic artery occlusion; CRAO: central retinal artery occlusion; BRAO: branch retinal artery occlusion; ION: ischemic optic neuropathy; HA: hyaluronic acid.

ATTACHMENT D

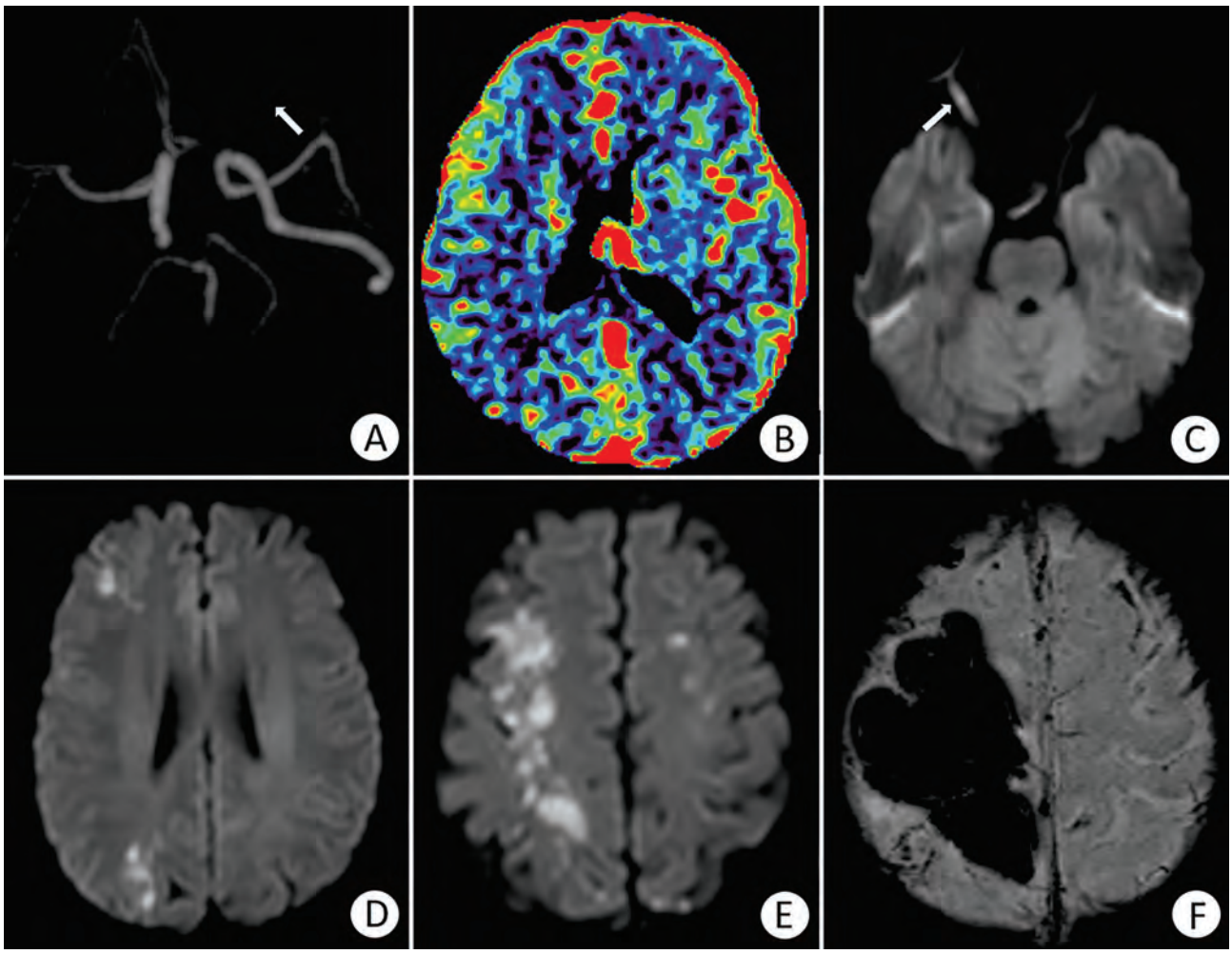


Figure 3. (**A**) CTA image of a patient 7.5 h after filler injection. The white arrow shows the normal left ophthalmic artery, while the right ophthalmic artery cannot be observed, reflecting its occlusion. (**B**) CT perfusion image showing that the time to peak perfusion was normal. (**C**) Diffusion-weighted imaging after 20 h showing a segmental hyperintense lesion in the thickened optic nerve of the right eye. (**D**, **E**) Diffusion-weighted imaging showing watershed infarctions in the bilateral frontal and parietal lobes and right occipital lobe. (**F**) Susceptibility-weighted image obtained after two days indicating postinfarction haemorrhage in the right cerebral hemisphere.

Discussion

Since the first cases of blindness occurring immediately after aesthetic filler treatments were reported in the 1980s[13], additional cases of filler injection-induced ophthalmic and cerebral complications have been reported. Only 34 articles describing blindness following aesthetic injectable treatment were found in the PubMed and Medline databases between 2000 and 2022[14]. However, few articles have reported the complete radiological appearance of cerebral and ocular complications. In this study, we summarized the clinical characteristics and radiological findings of twelve patients who received facial filler injections in association with vascular complications. Despite the more commonly involved OAO or its branch in all patients who underwent filler injection, cerebral infarctions on MRI were found in five patients. The radiological findings included filling defects in the MCA and flow stagnation in the distal branches of the ophthalmic artery on DSA, OA occlusion on CTA, optic nerve ischaemia, cerebral infarction on conventional brain MRI and haemorrhages on SWI.

Patients with HA-associated severe vascular complications of the eye and brain mostly present with symptoms such as blurred vision, headache, nausea, and vomiting[15]. The mechanism of vascular complications may be related to the abundance of anastomotic vessels and inappropriate surgical operation[16]. The blood supply in most facial injection areas mainly arises from the ophthalmic artery and internal carotid artery branches. The ophthalmic artery has multiple branches, such as the dorsal nasal artery, angular artery, supratrochlear artery and supraorbital artery, which anastomose with many other arteries in the face[17]. When injections are performed in facial areas, the tip of the needle may penetrate the artery; then, when the plunger pressure exceeds the systolic blood pressure, the filler can reverse the flow in the artery, moving as an embolus that propagates towards the origin of the ophthalmic artery, retinal artery, and internal carotid artery, subsequently reaching the cerebral circulation and causing brain damage[4,13]. The possible entrance of retrograde flow varies with the injection site:

ATTACHMENT D

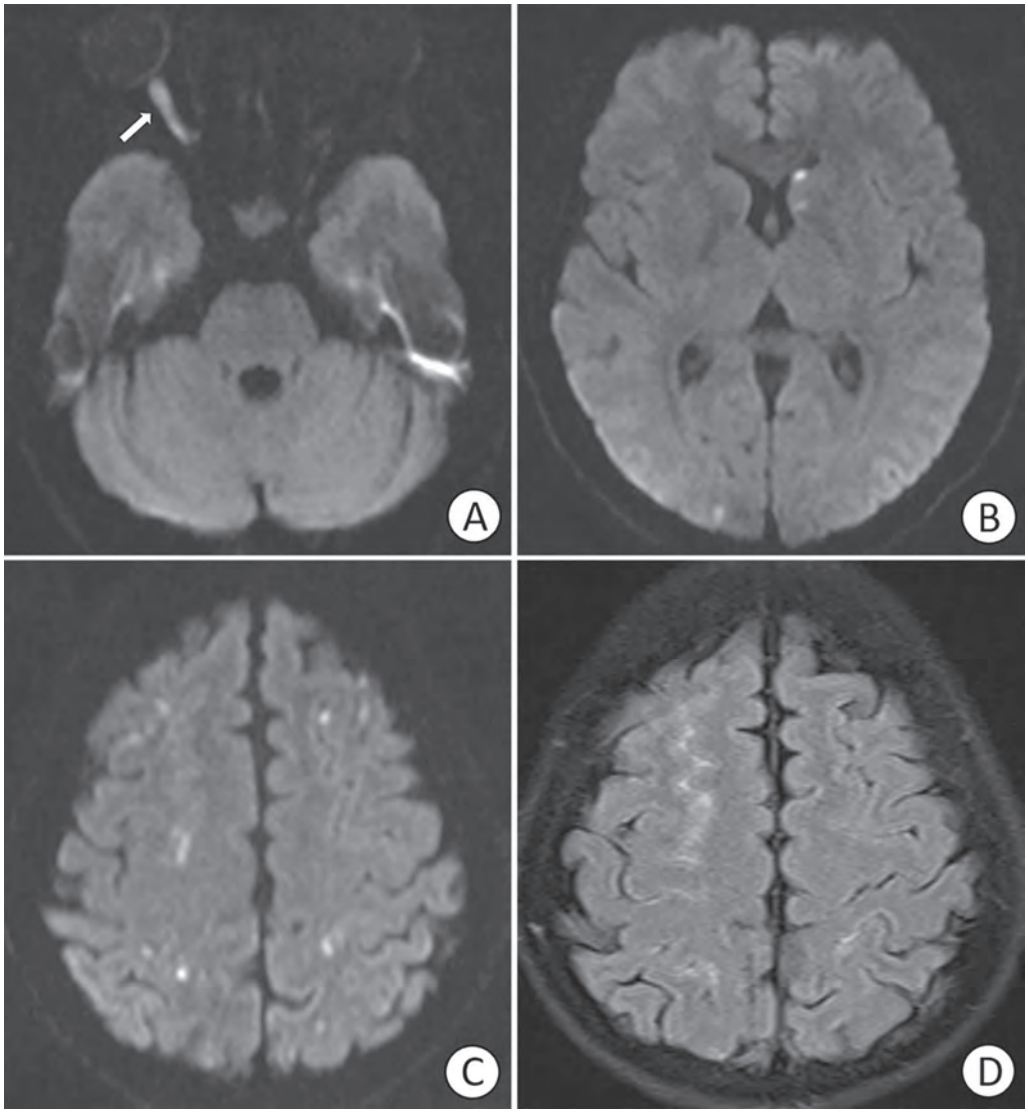


Figure 4. A 22-year-old female patient presented with a sudden loss of vision. (**A**) Diffusion-weighted imaging showing acute right optic nerve ischaemia. (**B**, **C**) Diffusion-weighted imaging showing scattered acute cerebral infarctions, mainly in the bilateral watershed areas. (**D**) Fluid-attenuated inversion recovery image showing subarachnoid haemorrhage.

The supratrochlear and supraorbital arteries are possible entry sites for retrograde blood flow in the glabellar and forehead regions. Anastomosis of the dorsal nasal artery from the ophthalmic artery, angular artery, or lateral nasal artery with the facial artery is the possible entry point for retrograde flow in the nose and nasolabial fold[18,19]. Occlusion of the ophthalmic artery was mostly reported due to injections in the nose, and six patients had optic nerve ischaemia, which may have been caused by the ophthalmic artery. However, occlusion of the retinal artery was mainly due to injections in the glabella. Three patients in this study received HA injections in the glabellae, and two of them developed clinical complications due to embolization of the retinal arteries, which is in accordance with the mechanism described above.

Two patients in our study who were injected on only one side of the face suffered bilateral cerebral infarction, possibly due to retrograde flow into the circle of Willis, through which the embolus arrived at the contralateral cerebral hemisphere, similar to the findings of a previous study[20]. Autologous fat causes unilateral permanent blindness more frequently than HA does. Compared with autologous fat, HA was reported by Park et al.[9] to be more likely to obstruct distal branches of the ophthalmic artery. However, unlike their report that large filling defects were only visible in fat-injected patients, in our HA-injected patients, large filling defects were found in the left MCA in Patient 3 and in the right OAO in Patient 2, illustrating that HA-related embolisms can also cause cerebral infarction and vision loss. One patient had a history of breast cancer, and a blood test showed a hypercoagulable state. Her left-eye blindness and intracranial hypertension occurred within 30 min of HA filler injection. We speculate that this may have been due to the complicated pathogenesis of hypercoagulation combined with HA injection. In a previous study[21], cerebral haemorrhage caused by superior sagittal sinus thrombosis

ATTACHMENT D

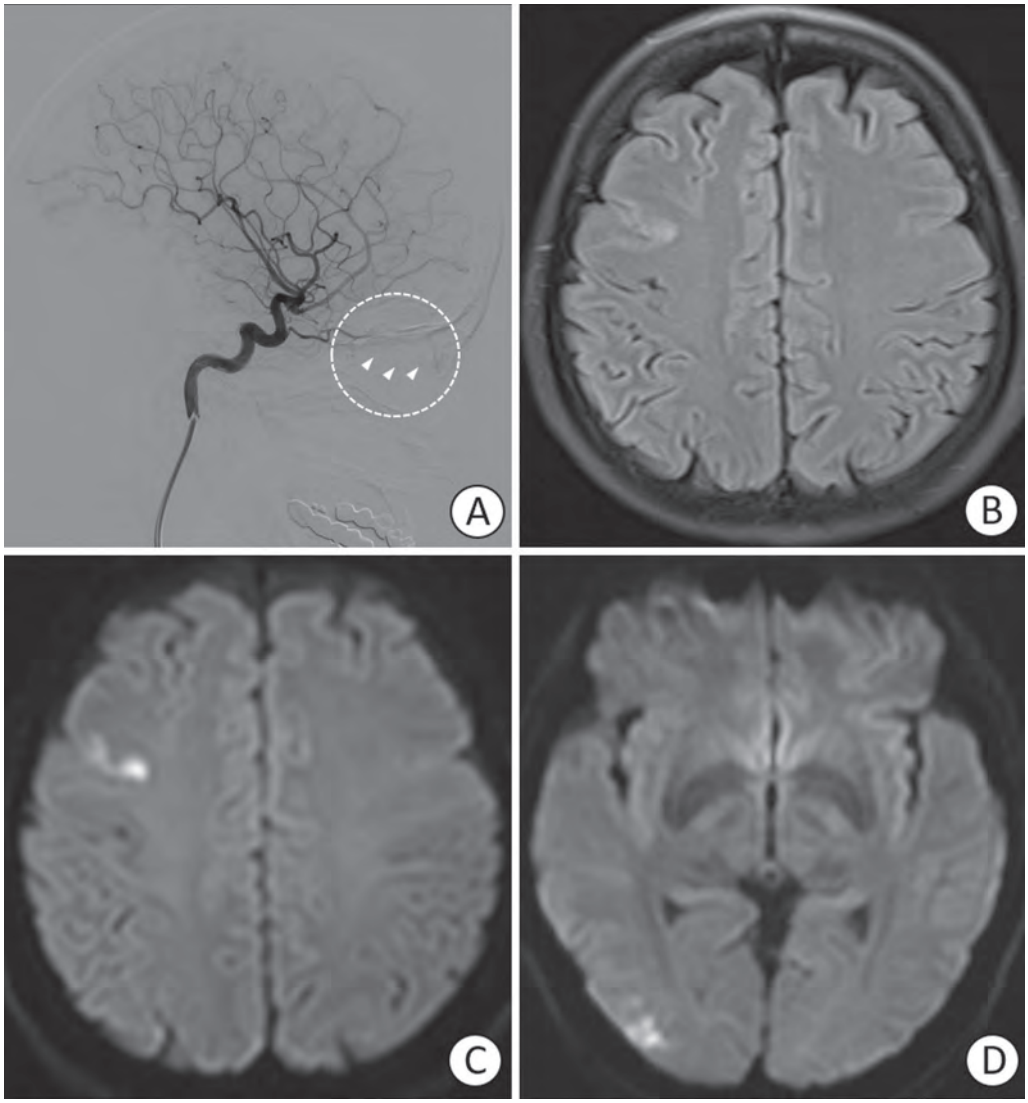


Figure 5. (**A**) Right internal carotid angiogram showing right central retinal artery occlusion, as shown by the circle and arrows. (**B**–**D**) Fluid-attenuated inversion recovery and Diffusion-weighted imaging indicating scattered acute infarctions in the right frontal and occipital lobes.

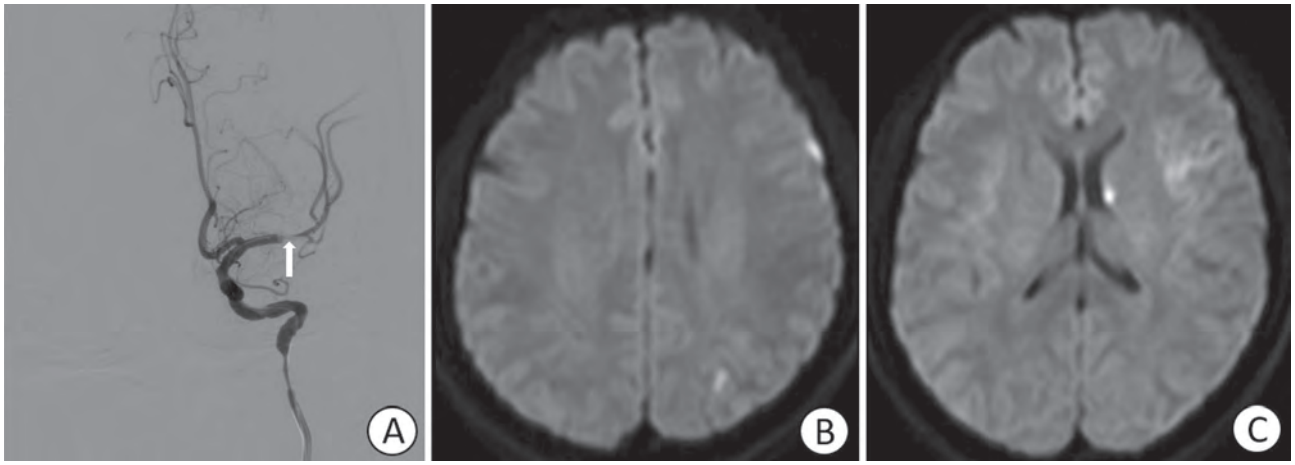


Figure 6. (**A**) The left internal carotid angiogram shows a filling defect in the left middle cerebral artery. (**B**, **C**) Diffusion-weighted images showing several small, acute foci of infarction in the left caudate nucleus and left frontal and parietal lobes.

ATTACHMENT D

immediately after HA injection was reported, possibly due to the erroneous injection of HA particles into veins during administration; these particles then passed through the venous system to the cavernous sinus due to the frontal vein plexus and the absence of a venous valve in the facial area, ultimately causing blockage in the superior sagittal sinus. All the patients in our study showed intracranial sinus normal, and no sinus thrombosis was observed. Cerebral haemorrhage after cosmetic facial injection has rarely been reported[22]; however, postinfarction haemorrhage formation and SAH were found in this case series, and the pathogenesis of these conditions remains unclear. Even with optimal medical therapy, malignant cerebral infarction is associated with up to 80% mortality in the first week[23]; however, Patient 2, who experienced cerebral haemorrhage after malignant cerebral infarction, was transferred to another hospital, and she was reported to have partly recovered at the 2-month follow-up. Three patients with cerebral infarction in this study underwent HBOT instead of thrombolysis because they were admitted to the hospital at that time for loss of vision and the cerebral infarction was subsequently detected on MRI, however, the time window for thrombolysis had passed. Nguyen NB et al. proposed HBOT is a non-drug treatment that could reduce functional symptoms, improve mobility, and reduce treatment time for patients with cerebral infarction[24].

According to a meta-analysis, cerebral infarction occurs in 12.9–24% of patients with serious complications after facial injections[25]. In a previous national survey by the Korean Retina Society[10], patients with cerebral infarction were found among those with occlusion of the ophthalmic artery and its branches following facial filler injections. Among thirty-one patients who underwent brain MR imaging, 12 (39%) had focal or multifocal brain infarctions; however, only six of these patients had concomitant neurologic symptoms, comprising contralateral hemiplegia and dysarthria. In our study, 5 of twelve patients (41.7%) had brain infarctions, and only three of them reported neurologic symptoms. Most patients suffer cerebral infarction during or shortly after surgery, however, five patients with a late onset of 9 h have been reported[26]. According to Xin L et al.[27], only 15% of patients confirmed with cerebral infarction by MRI or angiography have neurologic symptoms. In a previous study of multiple abnormal cerebral imaging changes in four out of ten patients with emotional disorder syndrome after cosmetic facial injection[28], the author speculated that the abnormalities on MRI might be attributed to cerebral infarction. In a study by Ansari et al.[20], one patient who reported no focal neurologic deficits was ultimately identified as having multifocal cerebral infarction on MRI. Similarly, Patients 1 and 6 showed no neurological deficits or symptoms, while MRI showed multifocal acute cerebral infarctions.

Filler-associated cerebral infarction has been more frequently observed in patients who had received autologous fat filler than in those who had received HA filler[14]. In this study, five-sixths of the patients were injected with HA, and nearly half of the patients (five out of twelve) suffered concomitant cerebral infarction, sometimes even bilateral or multifocal, on MRI. Eight CT scans performed for six patients after onset revealed no cerebral infarction or haemorrhage; however, the subsequent MRI showed multifocal acute/subacute cerebral infarctions. To obtain high-resolution imaging in soft tissue and sensitivity in detecting ischaemia, we strongly suggest that MRI should be performed at the earliest convenience to detect early ischaemia for early intervention even if no neurological symptoms are present. However, in this study, four patients with vision loss after filler injection did not undergo MRI scans because they presented no neurotic symptoms. It is believed that the actual incidence of cerebral ischaemia is higher than that reported, given that many HA filling surgeries are performed every year and because of the lack of brain MRI data for non-to-slightly symptomatic patients. It is necessary for patients who have visual loss to undergo an MRI scan for potential cerebral and optic nerve damage[29].

Although hyaluronidase can effectively degrade hyaluronic acid in the skin, the use of retrobulbar injections of hyaluronidase for reversing HA-related blindness remains controversial[30]. Theoretically, hyaluronidase could be useful for preventing HA-derived cerebral embolisms in the early stages. The appropriate dose of hyaluronidase is considered to be 2–4 mL (1500 U). Superselective intra-arterial thrombolysis has also been recently reported. Xiao et al. proposed that timely IATT is effective for ocular artery embolism caused by facial filler injections[8]. In our study, the endovascular administration of hyaluronidase alleviated occlusion of the ophthalmic artery and its branches in five patients, but only two patients experienced visual improvement after treatment. Thus, superselective angiographic delivery of hyaluronidase may have limited effects on reversing vision. Despite the use of hyaluronidase, the low recovery rate could be partially explained by the excessive gap between symptom onset and hyaluronidase injection, which ranged from 0.5 to 72 h in our study, with nine of the twelve patients exceeding the four-hour threshold. However, all the patients were transferred from other clinics, and a preoperative examination was needed, so it was difficult to manage the patients within the golden hour[31]. Zhang et al.[32] concluded that the combined use of hyaluronidase and urokinase is more effective than hyaluronidase alone. In-depth knowledge of the complex anatomy of the nose-eye-cerebral vasculature[4] and the use of a gentle technique for injecting the filler using the right pressure and selection of the proper region with a small volume are crucial factors to avoid serious consequences. Aspiration before injection might prevent retrograde embolization of the filler. Additionally, a blunt needle or cannula is recommended to avoid piercing into blood vessels and probable subsequent complications.

Despite the twelve valuable cases presented herein, this study has several limitations. First, a small population was included, although this sample size was larger than that of many previous case reports that included only one patient. Second, we excluded patients by searching for keywords in the electronic medical records, which may have introduced selection bias. Finally, not all patients underwent brain MR, as CT is not sensitive for detecting small early cerebral infarctions, and patients with brain damage may have been overlooked and underestimated.

In summary, cosmetic filler injections can result in emergent and catastrophic cerebral and ocular complications such as blindness and cerebral infarction. Initial radiological examinations, especially MRI, are crucial for detecting stroke, as some strokes may be asymptomatic. Awareness of severe complications may help both injectors to avoid vascular adverse events and clinicians in the treatment of complications immediately and properly.

ATTACHMENT D

Data availability

The authors declare that they had full access to all of the data in this study and that the authors take complete responsibility for the integrity of the data and the accuracy of the data analysis. The datasets used or analysed during the current study are available from the first author upon reasonable request.

Received: 28 October 2023; Accepted: 9 February 2024
Published online: 12 February 2024

References

1. Si, S. *et al.* A new injury severity scale for ocular complications following cosmetic filler injection. *Front Biosci (Landmark Ed)* **27**(2), 59 (2022).
2. Zhuang, J., Zheng, Q. & Hu, J. Dizziness and pain after temporal augmentation with hyaluronic acid. *J Craniofac Surg.* **34**(6), e590–e592 (2023).
3. Wu, Q. *et al.* Superselective ophthalmic artery thrombolytic therapy for hyaluronic acid embolization: a case report. *Clin Cosmet Investig Dermatol* **15**, 1459–1463 (2022).
4. Yang, Q. *et al.* Fatal cerebral infarction and ophthalmic artery occlusion after nasal augmentation with hyaluronic acid-a case report and review of literature. *Aesthetic Plast Surg* **44**(2), 543–548 (2020).
5. Nguyen, H. H. *et al.* Significant vision recovery from filler-induced complete blindness with combined intra-arterial injection of hyaluronidase and thrombolytic agents. *Aesthetic Plast Surg* **46**(2), 907–911 (2022).
6. Beleznay, K. *et al.* Avoiding and treating blindness from fillers: a review of the world literature. *Dermatol Surg* **41**(10), 1097–1117 (2015).
7. Kato, J. M. & Matayoshi, S. Visual loss after aesthetic facial filler injection: a literature review on an ophthalmologic issue. *Arq Bras Oftalmol* **85**(3), 309–319 (2022).
8. Xu, X. *et al.* Efficacy of intra-arterial thrombolytic therapy for vision loss resulting from hyaluronic acid filler embolization. *J Cosmet Dermatol* **20**(10), 3205–3212 (2021).
9. Kim, Y. K. *et al.* Cerebral angiographic findings of cosmetic facial filler-related ophthalmic and retinal artery occlusion. *J Korean Med Sci* **30**(12), 1847–1855 (2015).
10. Park, K. H. *et al.* Iatrogenic occlusion of the ophthalmic artery after cosmetic facial filler injections: a national survey by the Korean Retina Society. *JAMA Ophthalmol* **132**(6), 714–723 (2014).
11. Lee, K. E., Kim, G. J. & Sa, H. S. The clinical spectrum of periorbital vascular complications after facial injection. *J Cosmet Dermatol* **20**(5), 1532–1540 (2021).
12. Zhang, L. *et al.* Endovascular hyaluronidase application through superselective angiography to rescue blindness caused by hyaluronic acid injection. *Aesthet Surg J* **41**(3), 344–355 (2021).
13. AlGhadeer, H. *et al.* Acute unilateral vision loss and bilateral cerebral infarction following cosmetic filler injection. *Orbit* **42**(2), 185–188 (2023).
14. Mortada, H. *et al.* Ocular complications post-cosmetic periocular hyaluronic acid injections: a systematic review. *Aesthetic Plast Surg* **46**(2), 760–773 (2022).
15. Kapoor, K. M. *et al.* Vision loss associated with hyaluronic acid fillers: a systematic review of literature. *Aesthetic Plast Surg* **44**(3), 929–944 (2020).
16. Loh, K. T. *et al.* Prevention and management of vision loss relating to facial filler injections. *Singapore Med J* **57**(8), 438–443 (2016).
17. Wang, H. C. *et al.* Cerebral embolism as a result of facial filler injections: a literature review. *Aesthet Surg J* **42**(3), 162–175 (2022).
18. Park, S. W. *et al.* Iatrogenic retinal artery occlusion caused by cosmetic facial filler injections. *Am J Ophthalmol* **154**(4), 653–662 (2012).
19. Sito, G., Manzoni, V. & Sommariva, R. Vascular complications after facial filler injection: a literature review and meta-analysis. *J Clin Aesthet Dermatol* **12**(6), E65–E72 (2019).
20. Ansari, Z. A. *et al.* Ocular and cerebral infarction from periocular filler injection. *Orbit* **38**(4), 322–324 (2019).
21. Yao, B. *et al.* Ophthalmic artery occlusion combined with superior sagittal sinus thrombosis caused by hyaluronic acid injection for facial soft tissue augmentation: A case report. *Medicine (Baltimore).* **98**(36), e17048 (2019).
22. Wang, C. & Wang, X. Cerebral hemorrhage after cosmetic facial injection. *Plast Reconstr Surg Glob Open.* **7**(9), e2397 (2019).
23. Mohan, R. K. *et al.* Decompressive craniectomy for the treatment of malignant middle cerebral artery infarction. *Br J Neurosurg.* **31**(4), e2397 (2017).
24. Nguyen, N. B., Nguyen, T. H. H., Nguyen, S. T. & Nguyen, T. V. Results of acute cerebral infarction treatment with hyperbaric oxygen therapy. *Int Marit Health* **74**(4), 265–271 (2023).
25. Huang, Y. *et al.* Monophasic and biphasic hyaluronic acid fillers for esthetic correction of nasolabial folds: A meta-analysis of randomized controlled trials. *Aesthetic Plast Surg* **46**(3), 1407–1422 (2022).
26. Li, K. T. *et al.* Delayed-onset cerebral infarction after cosmetic facial injection using hyaluronic acid. *J Formos Med Assoc* **115**(7), 587–588 (2016).
27. Li, X., Du, L. & Lu, J. J. A novel hypothesis of visual loss secondary to cosmetic facial filler injection. *Ann Plast Surg* **75**(3), 258–260 (2015).
28. Wang, C. *et al.* Emotional disorder syndrome after cosmetic facial injection. *J Cosmet Dermatol* **19**(9), 2273–2276 (2020).
29. Lucaciu, A. *et al.* Sudden vision loss and neurological deficits after facial hyaluronic acid filler injection. *Neurol Res Pract* **4**(1), 40 (2022).
30. Adulkar, N. *et al.* An in vitro model assessing the penetration of hyaluronidase through optic nerve dura for management of hyaluronic acid facial filler embolism. *Plast Reconstr Surg* **144**(1), 43e–47e (2019).
31. Humzah, M. D. *et al.* The treatment of hyaluronic acid aesthetic interventional induced visual loss (AIIVL): A consensus on practical guidance. *J Cosmet Dermatol* **18**(1), 71–76 (2019).
32. Zhang, L. X. *et al.* Evaluation of intraarterial thrombolysis in treatment of cosmetic facial filler-related ophthalmic artery occlusion. *Plast Reconstr Surg* **145**(1), 42e–50e (2020).

Author contributions

F.F.Z. Conceptualization, design, acquisition of data, methodology, writing—original draft, writing—review and editing. Y.C. Conceptualization, formal analysis, writing—review and editing. D.H. Conceptualization, acquisition of data, formal analysis. X.X.Y. Conceptualization, methodology. Y.Y.X. Resources, design, methodology, funding acquisition, supervision, writing—review and editing.

Funding

This study was supported by the Natural Science Foundation of Zhejiang Province of China (LGF22H098112).

ATTACHMENT D

Competing interests
The authors declare no competing interests.

Additional information
Correspondence and requests for materials should be addressed to Y.X.

Reprints and permissions information is available at www.nature.com/reprints.

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Cerebral Embolism as a Result of Facial Filler Injections: A Literature Review

Aesthetic Surgery Journal
2022, Vol 42(3) NP162–NP175

DOI: 10.1093/asj/sjab193
www.aestheticsurgeryjournal.com
OXFORD UNIVERSITY PRESS

Hayson Chenyu Wang, MD; Nanze Yu, MD; Xiaojun Wang, MD; Ruijia Dong, MD; Xiao Long, MD; Xin Feng, MD; Jianle Li, MD; and Woffles T. L. Wu, MD

Abstract

Background: With the growth in the popularity of facial filler injections, increased numbers of severe adverse events, such as cerebral embolism, have been reported.

Objectives: The aim of this article was to summarize the clinical manifestations and proposed mechanisms of filler-induced cerebral embolism (FICE).

Methods: A literature review was performed with the search keywords "filler injection," "hyaluronic acid," "fat graft," "cerebral infarction," "cerebral embolism," "stroke," "cerebrovascular infarction," "disorders of consciousness," and "hemiplegia."

Results: Among the 43 cases of FICE enrolled from 35 articles, 37 patients were female, and 6 were male. Twenty-nine of these patients had received fat grafting, and 12 hyaluronic acid injection. Most FICE patients had been injected in the glabella, followed by the temporal, forehead, and nasal areas. Among 30 patients injected under local anesthesia, 43.33% presented with neurologic symptoms during the procedure. The main symptoms were consciousness disorders and hemiplegia. Most of the embolization sites were in the middle cerebral artery, followed by frontal lobe infarction and anterior cerebral artery infarction. Three patients developed cerebral hemorrhage after embolism. Twenty-six patients presented with newly acquired vision loss. The management for FICE cases included embolectomy, thrombolysis, decompressive craniectomy, antiplatelet/anticoagulant therapy, and symptomatic and nutritional treatment. Nearly half of the patients recovered or exhibited improved neurologic manifestations but not visual loss. Five patients died.

Conclusions: FICE is a severe complication following facial filler injection. Careful prevention, timely identification, and treatment are crucial to decreasing the morbidity and mortality of FICE.

Level of Evidence: 4

Editorial Decision date: March 22, 2021; online publish-ahead-of-print April 15, 2021.

AQ5

Facial contouring or volumization and the treatment of facial grooves, lines, depressions, or hollows can be achieved with synthetic off-the-shelf injectable facial fillers and autologous fat injections. Although the two techniques are conceptually and technically different, both are considered facial filler injections for the purposes of this review.

Injection of synthetic facial fillers is a widely used, minimally invasive facial cosmetic treatment that is increasing

Dr H.C. Wang is a chief resident, Dr Yu is an attending, Prof X. Wang is a director, Dr Dong is a medical student, and Prof Long is a deputy director, Division of Plastic Surgery, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China. Dr Feng is a resident, Department of Neurosurgery, Beijing Hospital, Beijing, China. Dr Li is a resident, Department of Neurology, The First Affiliated Hospital, Sun Yat-sen University, Guangzhou, China. Dr Wu is a plastic surgeon in private practice in Singapore.

Corresponding Author:
Dr Woffles T. L. Wu, Orchard Boulevard, Suite 09-02, Camden Medical Centre, Singapore 248649.
E-mail: woffles@woffleswu.com

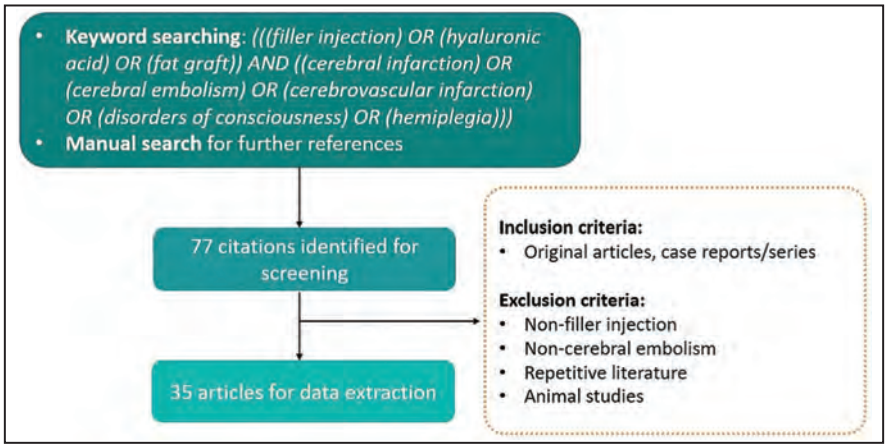


Figure 1. Flow diagram for study screening, selection, exclusion, and inclusion.

in popularity due to the ready availability, variety, ability to achieve natural outcomes, and perception of lower morbidity offered by these materials.[1] FDA-approved absorbable/temporary materials used in these fillers include hyaluronic acid (HA), collagen, calcium hydroxyapatite, poly-L-lactic acid (PLA),[2-4] and polymethylmethacrylate microspheres. The widely used term "dermal fillers" is actually a misnomer because most fillers can be placed at multiple levels of the soft tissue—subdermally, intramuscularly, or even deep on the periosteum. They should more correctly be called "soft tissue fillers."

Autologous fat harvested by liposuction is also used as a facial filler although this is more correctly classified as a tissue-grafting procedure or operation. It is frequently performed worldwide and more so in Asia where facial 3-dimensional contouring is popular. Although autologous fat can be considered a filler injection, the method of insertion for fat grafts differs from that of synthetic filler injections: the latter does not require blood supply. Collectively, these injectable facial fillers (synthetic or fat) are an option in the treatment of age-related soft tissue volume loss, depressed scars, facial sculpting and contouring, augmentation of specific anatomic sites, wound reconstruction, and atrophy or asymmetry caused by disease.[4]

Synthetic facial filler injections are considered relatively safe with short recovery times and little risk of complications. General anesthesia or sedation is not required and most patients can return to work immediately. Mild and temporary adverse events such as swelling, bruising, redness, surface deformity, and infection can occasionally occur after synthetic facial filler injections[1,4] and are acceptable risks. However, the increased use of synthetic facial injections has also led to a rise in reports of associated severe adverse events, such as hypersensitivity, cutaneous vascular complications with skin and tissue necrosis, blindness, and cerebral embolism.[1,5,6]

Facial fat injections, on the other hand, often require general anesthesia or intravenous sedation and are associated with higher rates of postoperative bruising, swelling, longer recovery times, and higher rates of morbidity that can include fat embolism and cerebral embolism.

Cerebral embolism associated with filler injections, whether by synthetic facial filler or facial fat injections, is a severe complication that has not received sufficient attention due to its low incidence rate and the lack of standardized approached to diagnosis, treatment, and prevention. The mechanism by which it occurs is not entirely clear and allows for healthy discussion. Here, we reviewed cerebral embolism cases induced by facial aesthetic filler injections, whether by synthetic fillers or fat grafting. We aimed to summarize the clinical manifestations, mechanisms, assessment, treatment, and prognosis of filler-induced cerebral embolism (FICE) patients, which may help clinicians understand this dreaded complication.

METHODS

For this study, a literature review was performed in June 2020 (H.C.W. conducted the search and N.Y. reviewed it) according to the guidance provided by Murad et al (Figure 1).[7] The following search terms were used in PubMed (United States National Library of Medicine [NLM], Bethesda, MD) to obtain all the relevant English-language literature published up to June 2020: "filler injection," "hyaluronic acid," "fat graft," "cerebral infarction," "cerebral embolism," "stroke," "cerebrovascular infarction," "disorders of consciousness," "hemiplegia." The relevant articles selected for this study included original articles and case reports/series that investigated or discussed the role of filler injection in cerebral infarction. The articles excluded from this study were those utilizing non-filler injection or those discussing complications other than cerebral embolism. Articles presenting cerebral embolism as posters/abstracts were excluded, and animal studies were also excluded. The following data were extracted from the articles: author(s), year of publication,

age and sex of patients, filler substance, injection site, anesthesia, symptoms and signs, onset time, diagnostic imaging results, infarction site, treatment, and prognosis. We were only able to analyze data captured in these articles, in some of which the reporting was incomplete.

RESULTS

There were 35 articles reporting 43 cases of FICE in total enrolled for data extraction according to our inclusion and exclusion criteria (Table 1).[5,6,8-40] Information about the publication year is shown in Figure 2.

Patients' Characteristics

Among the 43 cases, 37 patients were female and 6 patients were male. The age of the patients ranged from 19 to 65 years (mean, 33.93 years). Twenty-nine (67.4%) patients received fat grafting, 12 (27.9%) patients received HA injection, 1 patient received PLA injection, and 1 patient received hydroxyapatite injection. Thirty-five (81.4%) patients had 1 injection site, 7 (16.3%) patients received injections at multiple sites, and 1 patient's site was unknown. Of the 8 patients for whom the injection site was not specified, 6 (75%) received fat grafting. Data on the filler substance and injection sites are shown in Figure 3.

With regard to the clinical background of the patients, 30 (69.8%) patients were healthy, 3 patients had a history of eye conditions with visual loss due to cancer resection or trauma, 1 patient had hypertension, and the histories of 9 patients were unknown. Most of these cases were from East Asia.

Neurologic Manifestations

Regarding the neurologic manifestations (Figure 4), the main presenting symptoms were disorders of consciousness (n = 18) and hemiplegia (n = 16). Thirty (69.8%) patients received injections under local anesthesia, 6 (14.0%) patients received injections under general anesthesia, 2 patients received injections under intravenous sedation, and 5 patients' anesthesia information was unknown. Among the 30 patients receiving local anesthesia, 43.33% presented with neurologic symptoms during the procedure, and 16.67% presented with similar symptoms within 2 hours postprocedure (Figure 5).

Cerebral Embolism

To confirm a diagnosis of cerebral embolism, 26 patients underwent a magnetic resonance imaging scan, 12 patients underwent diffusion-weighted imaging, 8 patients underwent a computed tomography scan, 5 patients underwent computed tomography angiography, and 2 cases underwent superselective cerebrovascular angiography. Most of the embolization sites were at the middle cerebral artery (n = 29), followed by frontal lobe infarction (n = 14) and anterior cerebral artery infarction (n = 11) (Figure 6). Notably, 3 patients developed cerebral hemorrhage after embolism.

Vision Loss

Three patients had pre-existing visual loss (1 due to cancer resection, 2 due to orbital trauma). Of the 43 patients who suffered a FICE, 26 patients (60.5%) presented with concomitant vision loss and a stroke, whereas 17 patients (39.5%) presented only with FICE without any concomitant vision loss.

Among the 26 cases with vision loss, 5 patients receiving general anesthesia presented with vision loss after awakening, along with other neurologic signs. The remaining 21 patients had their procedures performed under local anesthesia: 10 of these patients (47.6%) presented with blindness and neurologic signs synchronously during or shortly postoperation (up to 2 hours). In 8 (23.8%) patients blindness appeared quickly postoperation, but their neurologic symptoms only occurred after several hours (at 4, 5, 8, 9, 24, 24, and 24 hours, respectively, and 1 case described as after "several hours"). The situation of 5 patients was unknown.

Among the 17 patients without concomitant vision loss, 5 patients (29.4%) had injections in the temporal area, 5 patients (29.4%) had injections in the glabella, 1 patient had injections in the forehead, 1 patient had an injection in the periocular region, 1 patient had an injection in the nasolabial folds, and 1 patient's injection site was unknown.

Treatment and Prognosis

The treatment of 28 patients was described in the literature (Figure 7). Seven patients underwent embolectomy and 2 patients underwent thrombolysis. Nine patients received decompressive craniectomy. Five patients underwent antiplatelet/anticoagulant therapy. The rest received only symptomatic treatment and nutritional treatment, including steroids, nutritional neuropharmaceuticals, mannitol, and hyperbaric oxygen. Regarding the prognosis, 21 (48.8%) patients recovered or improved neurologically (Figure 8). Five patients (11.6%) remained unimproved and 5 (11.6%) patients died.

DISCUSSION

Patients' Characteristics

The patients with FICE were predominantly females. Moreover, the vast majority of these patients were from

Table 1. The Data of the Enrolled Cases

Year	Author	Age/sex	History	Anesthesia	Filler	Site	Neurologic signs (onset time)	Vision loss	Infarction site	Treatment	Prognosis (follow-up time)
1993	Bitar et al[31]	47/F	Healthy	Local	Fat	Glabella	Agnosia, facial paralysis, hemiplegia (during the operation)	Right eye	Frontal lobe, parietal lobe, MCA	Not known	Improved (3 weeks)
1996	Lee et al[32]	42/F	Not known	Local	Fat	Nasolabial fold	Headache, consciousness disorder (during the operation)	Left eye	Caudate lobe, thalamus, left cerebral hemisphere cortex	Hyperbaric oxygen therapy	Improved (3 months)
1998	Feinendegen et al[33]	47/F	Healthy	General	Fat	Nasolabial folds, lip, chin	Hemiplegia, aphasia, consciousness disorder (7 hours postoperation)	No	Frontal lobe, temporal lobe, MCA	Not known	Improved (4 months)
2001	Danesh et al[34]	43/M	Not known	Local	Fat	Nose, nasolabial fold	Headache, aphasia, hemiplegia (10 minutes postoperation)	Left eye	MCA	Not known	Not known
2003	Yoon et al[35]	39/F	Healthy	Local	Fat	Glabella	Aphasia, hemiplegia, consciousness disorder (1 minute postoperation)	Left eye	left hemisphere, ICA	Mechanical ventilation, steroids	Death
2004	Thaunat et al[36]	39/M	Left eye cancer	Local	Fat	Temporal, eyelids, glabella	Consciousness disorder (during the operation)	NA	ACA	Not known	Improved (1 year)
2011	Lee et al[37]	44/F	Not known	Intravenous	Fat	Periocular area	Dysarthria (2 hours postoperation)	Left eye	Insula, MCA	Mannitol, hyperbaric oxygen therapy	No improvement
2010	Lee et al[38]	24/F	Not known	Intravenous	Fat	Forehead	Motor disturbance, paresthesias (1 day postoperation)	Left eye	MCA	Methylprednisolone	Improved (5 months)
2010	Toledano et al[39]	33/F	Eye wound	General	Fat	Left orbit	Hemiplegia (when awaking)	NA	MCA	Not known	Not known
2011	Hu et al[40]	28/F	Healthy	General	Fat	Temporal	Consciousness disorder, aphasia, hemiplegia (postoperation)	No	temporal lobe, parietal lobe, MCA	Mannitol, hydrocortisone, hyperbaric oxygen therapy, antiplatelet therapy	Improved (6 weeks)
2012	Park et al[41]	24/F	Healthy	Local	Fat	Glabella	Not known	Left eye	MCA	Not known	Not known
		26/F	Healthy	Local	Fat	Glabella	Not known	Left eye	MCA, ACA	Not known	Not known
2013	He et al[42]	52/F	Not known	Local	HA	Glabella	Headache (a few minutes postoperation)	Right eye	frontal lobe, occipital lobe, parietal lobe, ACA, MCA, PCA	Timolol maleate, acetazolamide, aspirin	Not known
2014	Hong et al[10]	27/F	Healthy	Local	Fat	Glabella, forehead, cheeks	Short-term memory disturbance, naming difficulty (several hours postoperation)	Left eye	frontal lobe	Not known	Improved mildly (1 year)
		50/F	Healthy	Local	HA	Glabella, cheeks	Dysarthria, hemiplegia, facial paralysis (24 hours postoperation)	Left eye	ACA, MCA, followed with cerebral hemorrhage at 2-week follow-up	Not known	Improved (6 months)
2014	Kim et al[23]	23/M	Not known	Local	HA	Nose	Right facial paralysis, left limb paralysis (during the operation)	Right eye	MCA, frontal, temporal and parietal lobes, followed by cerebral and subarachnoid hemorrhage by thrombolysis	Thrombolysis (plasminogen activator), decompressive craniectomy	No improvement (3 months)

Table 1. Continued

Year	Author	Age/sex	History	Anesthesia	Filler	Site	Neurologic signs (onset time)	Vision loss	Infarction site	Treatment	Prognosis (follow-up time)
2014	Kim et al[43]	Not known/F	Healthy	Local	HA	Nose	Not known	Right eye	Frontal lobe	Corticosteroids	Not known
2014	Hong et al[44]	31/F	Not known	General	Fat	Glabella	Arm weakness (24 h postoperation)	Right eye	MCA, frontal lobe, parietal lobe, temporal lobe, occipital lobe	Not known	Recover (5 months)
2014	Wang et al[45]	22/F	Healthy	General	Fat	Forehead, temporal	Hemiplegia, Babinski sign (+), aphasia (5 hours postoperation)	Left eye	ACA, MCA, ICA, ECA	Decompressive craniectomy	Improved (2 months)
2015	Roshandel et al[46]	65/F	Hypertension	Not known	Fat	Forehead	Hemiplegia (several hours postoperation)	Right eye	frontal lobe, parietal lobe, occipital lobe, MCA	Not known	Not known
2015	Lin et al[47]	25/F	Healthy	Local	HA	Nose	Nausea, dizziness, weakness (4 hours postoperation)	Right eye	MCA	Not known	Not known
2019	Wang et al[5]	49/F	Healthy	Local	HA	Forehead	Consciousness disorder, headache, hemiplegia (during the operation)	No	Temporal, frontal and parietal lobes, followed with cerebral and subarachnoid hemorrhage	Low-molecular-weight heparin, clopidogrel, mannitol	Death
2016	Shen et al[14]	30/F	Healthy	Local	Fat	Temporal, chin	Consciousness disorder, left limb weakness, incontinence, vomiting (8 hours postoperation)	No	Right brain hemisphere, ICA, ECA, CCA, MCA, superficial temporal artery	Lowering intracranial pressure, antiplatelet aggregation, decompressive craniectomy	Improved (2 months)
2016	Kang et al[48]	32/F	Healthy	Local	Fat	Glabella	Consciousness disorder, aphasia, hemiplegia (during the operation)	Left eye	ACA, MCA	Thrombolytic agents	Improved (3 months)
2016	Li et al[49]	25/F	Healthy	Local	HA	Nose	Left upper limb weakness (9 hours postoperation)	Right eye	MCA	Not known	Not known
2017	Ragam et al[19]	55/F	Healthy	Local	PLA	Forehead	Dizziness, weakness, consciousness disorder (during the operation)	Right eye	ACA, frontal lobe, corpus callosum	Methylprednisolone	No improvement
2018	Marumo et al[50]	26/F	Healthy	Local	Hydroxyapatite	Glabella	Nausea, diplopia, consciousness disorder (during the operation)	Left eye	ECA	Not known	Not known
2020	Zhang et al[24]	31/F	Not known	Local	HA	Nose	Headache, nausea and vomiting, incontinence (5 minutes postoperation)	Left eye	MCA	Steroids, hyperbaric oxygen therapy, EHATSA	Improved
		46/F	Not known	Local	HA	Palpebra superior	Emotional disorder (hyperactivity) (not known)	Right eye	Lacunar cerebral infarction	Glucocorticoids, neurotrophic drug, hyperbaric oxygen, EHATSA	No improvement
2020	Liu et al[51]	35/F	Healthy	Not known	Fat	Not known	Hemiplegia (during the operation)	No	MCA, ECA	Aspirin, atorvastatin, dexamethasone	Recover (3 months)
2020	Yang et al[6]	40/F	Healthy	Local	HA	Nose	Nausea, vomiting, headache, consciousness disorders (30 minutes postoperation)	Left eye	Frontal lobe, parietal lobe, temporal lobe, occipital lobe	Mannitol, glucocorticoid, mechanical ventilation	Death
2020	Wang et al[7]	32/F	Healthy	Local	HA	Glabella	Emotional disorder (not known)	No	Frontal lobe	Antidepression therapy	Improved

Table 1. Continued

Year	Author	Age/sex	History	Anesthesia	Filler	Site	Neurologic signs (onset time)	Vision loss	Infarction site	Treatment	Prognosis (follow-up time)
2019	Zhou et al[26]	22/F	Healthy	Local	Fat	Temporal	Hemiplegia, consciousness disorder (4 hours postoperation)	No	ICA, MCA	Mechanical thrombectomy + thrombus aspiration technique	Improved (3 months)
2019	Ansari[9]	20/F	Healthy	Local	HA	Glabella	None	Right eye	parietal lobe, circle of Willis	Aspirin, prednisone	NA
2019	Liu et al[17]	42/F	Healthy	Local	Fat	Temporal	Lethargy, aphasia, hemiplegia (during the operation)	No	ICA, ACA, MCA, frontal, temporal and parietal lobes, superficial temporal artery	Decompressive craniectomy	No improvement (2 years)
2019	Renard et al[52]	50/M	Eye wound	General	Fat	Right orbit	Hemiplegia (when awaking)	NA	ACA, MCA	Not known	Not known
2018	Huo et al[18]	33/F	Healthy	Local	Fat	Glabella	Motor disturbance, consciousness disorder (during the operation)	No	ICA, MCA	Embolectomy + decompressive craniectomy	Improved
		25/F	Healthy	Local	Fat	Glabella	Motor disturbance, consciousness disorder (during the operation)	No	MCA, ACA, frontal, and temporal lobes	Embolectomy + decompressive craniectomy	Improved
		24/F	Healthy	Not known	Fat	Periocular	Seizure, consciousness disorder, motor disturbance (2 hours postoperation)	No	ACA, CCA, ICA, MCA, PCA	Embolectomy	Death
		19/M	Healthy	Not known	Fat	Glabella	Hemiplegia, consciousness disorder (1 hour postoperation)	No	MCA	Embolectomy + decompressive craniectomy	Improved
		28/M	Healthy	Not known	Fat	Glabella	Seizure, consciousness disorder (5 hours postoperation)	No	Not known	No	Death
2018	Wang et al[16]	22/F	Healthy	Local	Fat	Temporal	Consciousness disorder, limb weakness (during the operation)	Both	MCA, superficial temporal artery	Decompressive craniectomy	Improved (2 years)
		30/F	Healthy	Local	Fat	Temporal	Weakness (during the operation)	No	Right hemisphere, superficial temporal artery	Decompressive craniectomy	Not known

ACA, anterior cerebral artery; CCA, common carotid artery; ECA, external carotid artery; EHATSA, endovascular hyaluronidase application through superselective angiography; ICA, internal carotid artery; MCA, middle cerebral artery; NA, not available; PCA, posterior cerebral artery.

East Asia (only 9 out of 35 papers were from the West). This gender and ethnic bias may reflect the aesthetic aspirations of many Asian women today who wish to achieve an oval or heart-shaped face with smooth, full, and convex forehead contours and an absence of temporal hollows.[41] This aesthetic trend has led to an increase in the use of autologous fat or synthetic fillers to create the desired convex shape. The forehead, brow, and temples are well-established danger zones where numerous arterial connections between the internal and external carotid artery systems exist as well as terminal arterial branches of the ophthalmic artery. These can be inadvertently punctured, leading to a filler embolus entering the internal carotid artery system, and may explain why so many patients with FICE are in fact Asian and women. Males, whether Asian or Caucasian, are less interested in shaping their foreheads and temporal regions, which may explain their lower risk for this severe adverse event.

Clinical Manifestations

The clinical manifestations of FICE were mainly neurologic symptoms and signs related to the location and degree

of the obstruction, including hemiplegia and consciousness disorders. In the literature, the symptoms of some patients with mild obstruction were less recognizable, and were identified as obstruction by further imaging examinations. These patients sometimes presented with neuropsychiatric symptoms only, such as emotional or mood changes, memory disturbance, or asymptomatic lacunar infarction, which was seen only on imagings.[8,13,37,39] Therefore, we speculate that the incidence of FICE may be much higher than that reported in the literature. We also noticed that the recognition of the onset of cerebral embolism symptoms was affected or delayed by the type of anesthesia used.

Generally, neurologic symptoms occurred during the operation or within 1 hour postoperation for the FICE patients receiving filler injection under local anesthesia. However, it took more time for the patients under general/intravenous anesthesia to complain about neurologic symptoms because they needed time to wake up from anesthesia. This may delay the timely diagnosis of cerebral embolism. Therefore, to detect cerebral embolism in time, patients recovering from general/intravenous anesthesia should be closely examined for neurologic signs, including muscle strength, muscle tension, pupillary light reflection, and pathologic reflexes.

In addition, due to the fact that a considerable number of patients with cerebral embolism were associated with immediate blindness, or even delayed blindness, which in turn was related to the mechanism of emboli entering the internal carotid or ophthalmic blood vessels at different times, those patients who complain only of ocular symptoms should also be carefully evaluated for signs and symptoms of cerebral embolism as well. We have noted 8 cases where the neurologic signs developed between 4 and 24 hours postoperatively.

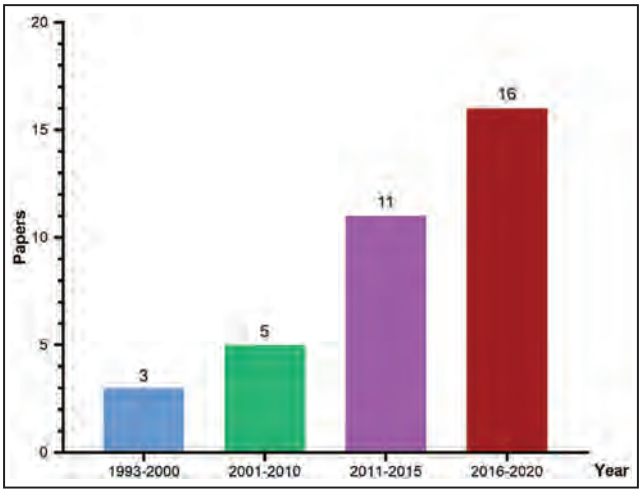


Figure 2. Publications reporting filler-induced cerebral embolism have increased over time.

Mechanism

In the literature the most frequent injection site associated with FICE was the glabella, followed by the temporal, forehead, and nasal areas. At present, it is thought that FICE and blindness is a direct result of accidental injection of filler material into a facial vessel that is a terminal branch of the ophthalmic artery (internal carotid artery system) or into a branch of the facial artery (external carotid artery system) that, in turn, anastamoses with branches of the internal carotid artery system. This leads to subsequent retrograde embolism and obstruction of certain cerebral vessels or the ophthalmic artery branches.

By analyzing the imaging findings of the FICE patients reported in the literature, we summarized the possible

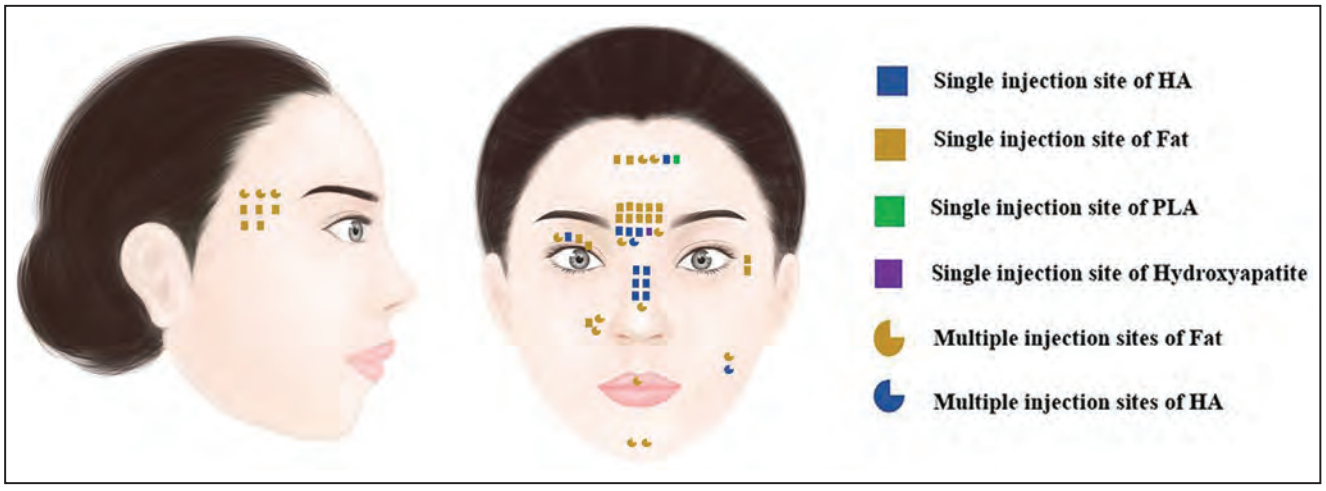


Figure 3. Filler substances and injection sites. HA, hyaluronic acid; PLA, poly-L-lactic acid. Artwork created by author H. C. Wang, reproduced with permission from the author.

ways of the filler leading to intracranial vascular embolism into 3 types, which are described in Table 2.

One possible mechanism is that during the injection procedure, the filler material was inadvertently injected under pressure into one of the extracranial terminal branches of the ophthalmic artery (supratrochlear, supraorbital, dorsal nasal, anterior ethmoidal, and lacrimal arteries) or injected into any of the anastomotic branches between the internal carotid and external carotid artery systems (Figure 9). Filler emboli may then reach the ophthalmic artery and/or the internal carotid artery. Blindness occurred when the central retinal artery (CRA), or posterior ciliary artery (PCA) was obstructed, whereas cerebral embolism occurred when the terminal intracranial branches of the internal carotid artery were obstructed (Figure 10).

It is a known anatomic fact that many anastomotic branches exist between the external and the internal carotid artery systems, and although there is significant human variation, 4 main groups of these anastomotic vessels are described:[42]

(1) The frontal (anterior) branch of the superficial temporal artery anastomoses with the lacrimal, palpebral, or supraorbital branches of the ophthalmic artery.
(2) The angular artery is a terminal branch of the facial artery, which is in turn derived from the external maxillary artery (external carotid artery system). The angular artery can anastomose directly with the inferior palpebral artery, the dorsal nasal artery, or the supratrochlear artery, all of which are terminal branches of the ophthalmic artery (internal carotid artery system). The supratrochlear or anterior ethmoidal arteries may continue down the dorsum of the nose as the dorsal nasal artery, which often anastomoses with the alar and sidewall branches of the facial artery.[43]
(3) The orbital branches of the middle meningeal pass through the superior orbital fissure, and anastomose with the lacrimal or other branches of the ophthalmic artery.
(4) The infraorbital branch of the internal maxillary artery may anastomose with the dorsal nasal branch of the ophthalmic artery.

It must be appreciated that there are many arterial and anastamotic variations, with some individuals having one and not the other, or even having multiple of these connections.

Whichever of these direct or anastamotic routes is traversed, it is reasonable to assume that a column of filler material must first find its way into either the dorsonasal,

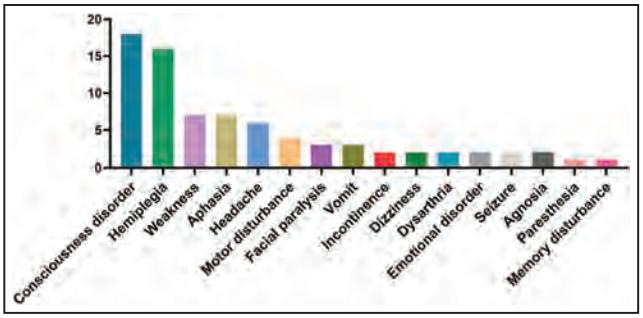


Figure 4. Neurologic manifestations.

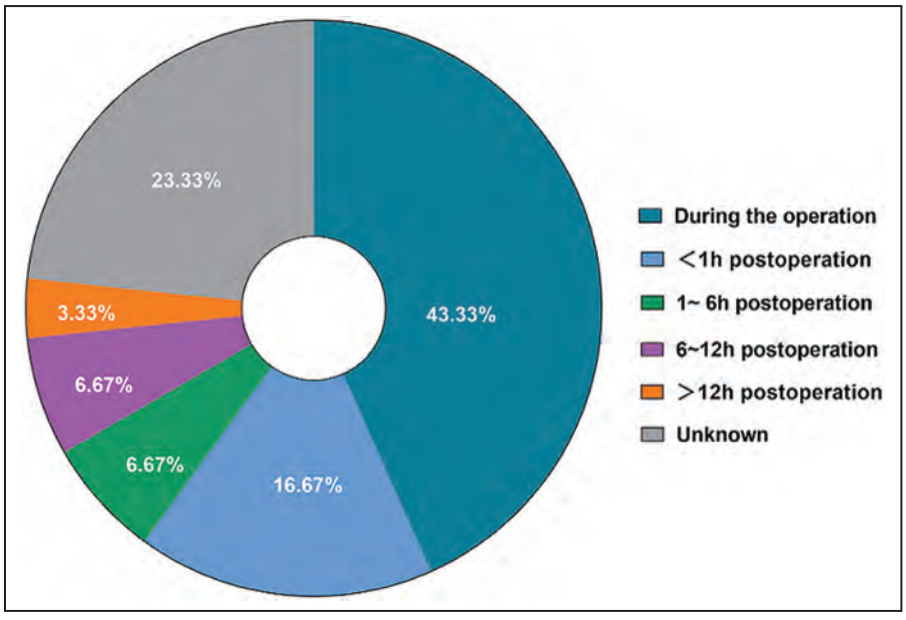


Figure 5. The onset of neurologic manifestations in 30 patients receiving filler injections under local anesthesia.

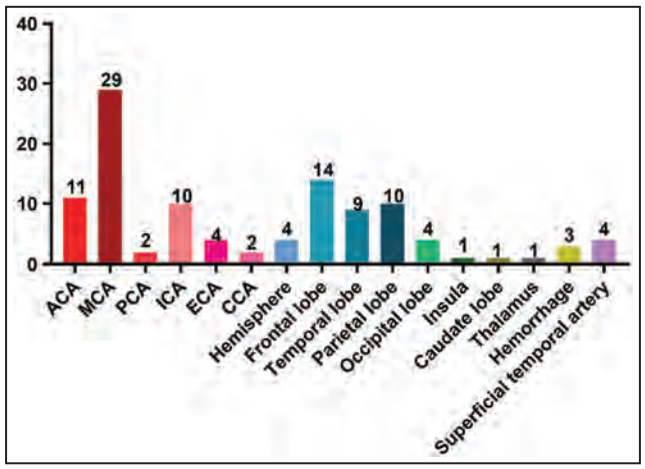


Figure 6. Embolization sites. ACA, anterior cerebral artery; CCA, common carotid artery; ECA, external carotid artery; ICA, internal carotid artery; MCA, middle cerebral artery; PCA, posterior cerebral artery.

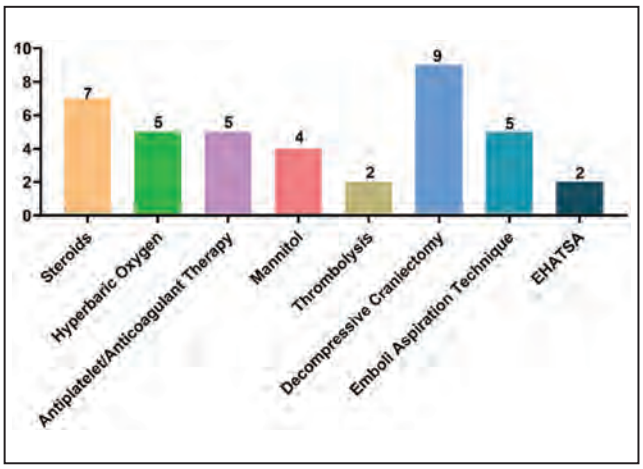


Figure 7. Filler-induced cerebral embolism treatment. EHATSA, endovascular hyaluronidase application through superselective angiography.

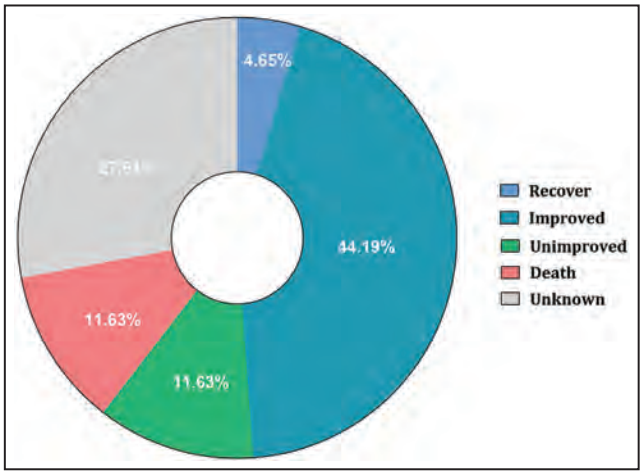


Figure 8. The prognosis of the filler-induced cerebral embolism patients.

supratrochlear, or supraorbital arteries (all being externalized terminal branches of the ophthalmic artery) before it is forced retrogradely into the ophthalmic artery itself, past the origins of the central retinal and posterior ciliary arteries[44] and subsequently past the origin of the ophthalmic artery from the internal carotid artery.

If the column of filler material is sufficient to go past where the CRA and PCA originate from (Figure 10) but not into the internal carotid artery, then that embolus may be carried anterogradely down the CRA or PCA and give rise to visual disturbances. A cerebral embolism would not occur in this situation.

If, however, the filler material traverses the entire length of the ophthalmic artery and enters the internal carotid artery, it can then potentially be carried anterogradely downstream until it reaches the middle cerebral artery or other intracranial vessels that derive from the internal carotid artery, and then eventually obstructs a terminal branch in the brain.

In Table 2, this is referred to as the Type I mechanism for cerebral embolism. This type of vascular embolism can cause immediate cerebral embolism and/or blindness. It has been shown in experimental and anatomic models that as little as 0.08 mL of HA filler can cause blindness.[44] It is not known how much filler is required to induce a cerebral embolism.

In the Type II mechanism of cerebral embolism, the superficial temporal artery is injured during temporal injections. After entering the superficial temporal artery, the filler emboli may be pushed into the external carotid artery or even the common carotid artery under excessive injection pressure, which then flows into the internal carotid artery and the intracranial blood vessels, resulting in cerebral embolism and/or blindness.[25,32,36,45] This kind of embolization can be preliminarily confirmed by loss of pulsation of the superficial temporal artery on palpation.[16]

The Type III mechanism occurs when the veins of the face are damaged during the injection process. The filler then embolizes to the heart first, after which it follows the systemic circulation, before it reaches the terminal branches and causes vascular complications, such as pulmonary embolism, cerebral embolism, or blindness.[29,46-48] The manifestations of this type of vascular embolism may present hours after the initial injection;[29,46] multiple factors, such as overinjection, injection displacement, muscle activity, and other factors, may also play a role in vascular complications of filler injection.

Table 2. Three Possible Ways for Filler to Lead to Intracranial Vascular Embolism

Type	Mechanism	Route by which emboli enter the brain	Onset of neurologic signs	Other possible manifestations
I	The filler emboli enter the extracranial branches of the ophthalmic artery injured during the injection, or the anastomotic branches of the internal carotid artery and the external carotid artery injured during the injection	Extracranial branches of ophthalmic artery/anastomotic branches of ICA and ECA → ophthalmic artery → MCA	Immediate	Blindness
II	The filler emboli enter the superficial temporal artery, the filler emboli may be pushed into the external carotid artery or even the common carotid artery under excessive injection pressure	Superficial temporal artery → ECA → CCA → ICA → MCA	Immediate	Blindness
III	The filler emboli enter veins damaged during the injection	Veins on face → anterograde venous system → heart → brain/lung/eye	Delay	Delayed blindness, pulmonary embolism

CCA, common carotid artery; ECA, external cerebral artery; ICA, internal carotid artery; MCA, middle cerebral artery.

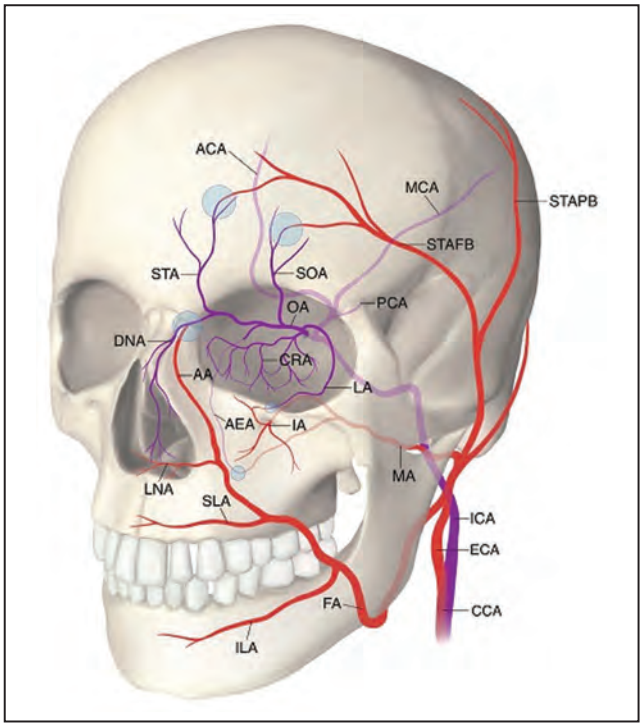


Figure 9. Schematic diagram showing the extracranial branches of the ophthalmic artery and the anastomotic branches (purple circle) of the internal carotid artery (blue) and the external carotid artery (red). AA, angular artery; ACA, anterior cerebral artery; AEA, anterior ethmoidal artery; CCA, common carotid artery; CRA, central retinal artery; DNA, dorsal nasal artery; ECA, external carotid artery; FA, facial artery; IA, infraorbital artery; ICA, internal carotid artery; ILA, inferior labial artery; LA, lacrimal artery; LNA, lateral nasal artery; MA, maxillary artery; MCA, middle cerebral artery; OA, ophthalmic artery; PCA, posterior cerebral artery; SLA, superior labial artery; SOA, supraorbital artery; STA, supratrochlear artery; STAFB, superficial temporal artery frontal branch; STAPB, superficial temporal artery parietal branch. Artwork created by author R. Dong, reproduced with permission from the author.

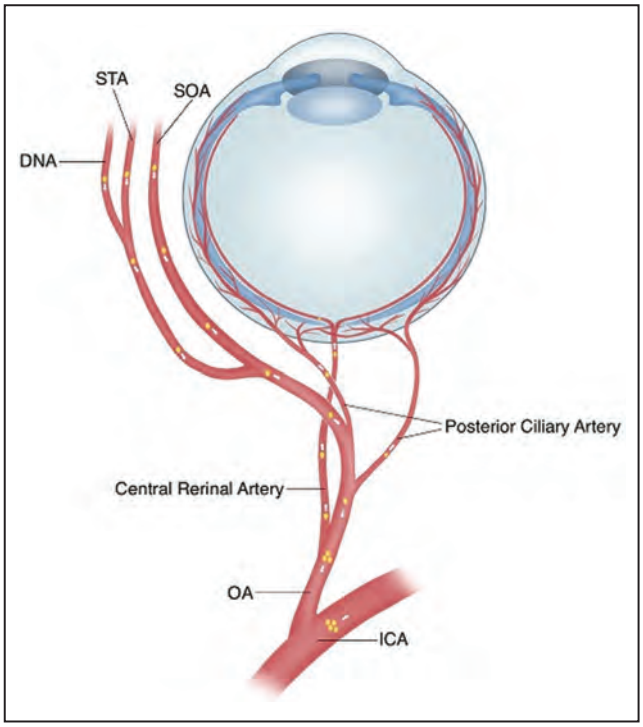


Figure 10. Schematic diagram showing the relation between blindness and cerebral embolism. CRA, central retinal artery; DNA, dorsal nasal artery; ICA, internal carotid artery; OA, ophthalmic artery; SOA, supraorbital artery; STA, supratrochlear artery. Artwork created by author R. Dong, reproduced with permission from the author.

Cannula vs Sharp Needle

The debate over which one of these modalities is safer continues. It was initially thought that a blunt cannula would be a safer instrument than a sharp needle for facial filler injections. However, both cannulas and sharp needles have been seen to penetrate blood vessels and cause filler emboli.

A more important consideration would be at which level of soft tissue (subdermal, superficial fat, fascia, muscle, deep fat, or periosteum) these fillers were injected and whether there are major blood vessels in the vicinity that could potentially be penetrated by either of these instruments.

The 35 articles surveyed for this systematic review are silent on the use of cannulas but it can safely be assumed that in all the patients who received facial fat injections (29 out of 43, 67.4%) the injections would have been performed with a cannula, as is the usual practice. Of the 12 patients who received HA filler injections (27.9%), we can also extrapolate that at least 50% of these would have been administered by a cannula. This implies that up to 82% of all FICE cases may have been associated with the use of a cannula.

This alarming statistic could be due to the very nature of facial fat injections as they require the fat to be delivered in multiple passes and evenly distributed throughout the middle lamellar (muscle) of the soft tissue so as to allow a blood supply to develop. In the face, the arteries lie mainly in or just deep to the middle lamella of facial muscles, and therefore multiple passes of the cannula in this layer increase the risk of vascular damage and penetration.

With regard to the depth of injection, detailed knowledge of facial anatomy would suggest that the subdermal and/or supraperiosteal layers are safer for injection because there are few major arteries running in these 2 layers. In our opinion, it makes sense to inject immediately subdermally in the subcutaneous fat or deep on the bone (avoiding the vascular bony foramina such as the infraorbital or supraorbital foramen) to reduce inadvertent penetration of the blood vessels (such as the facial or superficial temporal arteries) which are more intimately associated with the layer of facial muscles (the middle lamella). Injecting into either the subdermal or preperiosteal layers is possibly easier to achieve with a sharp needle than a cannula. A cannula may provide the injector with a false sense of security, leading to more vascular trauma.

Treatment

The current treatment of FICE includes general symptomatic and nutritional therapies such as hyperbaric oxygen, neuropharmaceuticals, mannitol, and steroids. Thrombolytic therapy or antiplatelet/anticoagulant therapy is not only ineffective for patients with cerebral embolism induced by filler injection (which is a nonthrombotic embolism), it may also cause drug-induced cerebral hemorrhage, aggravating the patient's condition.[5,19] For vascular embolism caused by HA, some researchers have tried to achieve recanalization of the occluded vessel by administering intra-arterial thrombolysis therapy with the injection of hyaluronidase and/or urokinase. In a study of 24 patients with vision loss caused by HA injection, 42% of the patients ultimately showed improvements in visual acuity following intra-arterial thrombolysis therapy even when the recommended window for optimal thrombolytic treatment had passed.[49] In addition, the authors found that hyaluronidase combined with urokinase was a more effective therapy than hyaluronidase alone. In cases of filler-induced blindness, we know that extravascular or retrobulbar hyaluronidase plays little or no role in resolving visual loss.[44,50] For embolization due to fat, some researchers have used an emboli aspiration technique to partially recanalize the occluded vessel; however, this technique carries the potential risk of triggering distant cerebrovascular embolism.[16,40]

The prognosis of FICE is related to which vessels are occluded. Unlike the obstruction of small blood vessels leading to mild symptoms with a good prognosis, occlusion of large blood vessels can lead to a large-area cerebral infarction with secondary exacerbation of the edema, which was associated with high morbidity and high mortality.[18] Under such circumstances, decompression craniectomy is strongly recommended to reduce mortality.[16] It is crucial for FICE patients to be diagnosed and treated in time. Delayed treatment may also lead to poor prognosis.[16,40]

Prevention

With treatment options for FICE being somewhat limited, and to an extent ineffective, it would be prudent for practitioners around the world to be acutely aware of this complication and take the necessary steps to reduce its occurrence. From the papers sourced for this review, we notice a worrying trend in the occurrence of FICE. Between 1993 and 2010 (17 years) 8 cases of FICE were reported. This jumped to 11 cases between 2011 and 2015 (4 years) and a further jump to 16 cases in the period 2016 to 2020 (4 years). This means that in the last 8 years the total number of FICE cases has risen to 27, more than 3.5 times that in the period 1993 to 2010 (Figure 2).

Most of these cases were from East Asia and the majority were associated with facial fat injections with cannulas. This alarming increase in the frequency of FICE occurrence may reflect the current situation where there is a proliferation of underground illegal cosmetic clinics in

this region. Here, untrained operators without a semblance of understanding of anatomy are more likely to damage blood vessels when injecting filler.

For medical practitioners performing these procedures, some measures have been widely recommended to reduce the incidence of vascular complications during the injection process. These include: (1) aspirating and maintaining negative pressure upon entry all the way to the designated site; (2) injecting small volumes slowly while closely observing the injection site and the patient's reaction—physicians should avoid using too many fillers at one time; (3) injecting filler with blunt cannulas rather than needles. This last point is arguable because it flies in the face of the evidence we have—over 80% of FICE patients in this review were likely treated with cannula injections. This therefore contradicts the dictum that "cannulas are safer." In fact, delivering filler directly to the bone with a sharp needle may provide a safer alternative than cannulas which may give the injector a false sense of security.

We submit that, for injecting fillers, the critical skill a medical practitioner should possess is a sound knowledge of facial anatomy—so that they know the course and changing levels of the major vessels, have an understanding of the sites of anastomosis between internal and carotid artery systems, and are familiar with the different soft tissue layers and their relations with the arteries of the face.[51]

Even then, these measures may still fail to completely avoid the occurrence of filler-associated vascular complications, due to multiple factors such as anatomic variations and operator skill. The development of ultrasound-assisted injection may allow practitioners to clearly recognize the location of blood vessels in relation to the different anatomic layers[52-54] of soft tissue. The use of ultrasound-assisted injections, although requiring training, is not that complicated to master. This may be the trend for filler injection methods in the future. We also recommend performing filler injections under local anesthesia as much as possible in order to identify and treat FICE in a timely manner.

CONCLUSIONS

FICE is a severe complication following facial filler injection with limited treatment options. Careful prevention and timely identification and treatment are crucial to decrease the morbidity and mortality of FICE.

Disclosures

The authors declared no potential conflicts of interest with respect to the research, authorship, and publication of this article.

Funding

Dr Hayson Chenyu Wang was supported by the China Scholarship Council (201906210435).

REFERENCES

1. Kapoor KM, Kapoor P, Heydenrych I, Bertossi D. Vision loss associated with hyaluronic acid fillers: a systematic review of literature. *Aesthetic Plast Surg.* 2020;44(3):929-944.
2. Massone C, Horn M, Kerl H, Ambros-Rudolph CM, Giovanna Brunasso AM, Cerroni L. Foreign body granuloma due to Matridex injection for cosmetic purposes. *Am J Dermatopathol.* 2009;31(2):197-199.
3. Grippaudo FR, Mattei M. High-frequency sonography of temporary and permanent dermal fillers. *Skin Res Technol.* 2010;16(3):265-269.
4. Wang C, Sun T, Li H, Li Z, Wang X. Hypersensitivity caused by cosmetic injection: systematic review and case report. *Aesthetic Plast Surg.* 2021;45(1):263-272.
5. Wang C, Wang X. Cerebral hemorrhage after cosmetic facial injection. *Plast Reconstr Surg Glob Open.* 2019;7(9):e2397.
6. Yang Q, Lu B, Guo N, et al. Fatal cerebral infarction and ophthalmic artery occlusion after nasal augmentation with hyaluronic acid—a case report and review of literature. *Aesthetic Plast Surg.* 2020;44(2):543-548.
7. Murad MH, Sultan S, Haffar S, Bazerbachi F. Methodological quality and synthesis of case series and case reports. *BMJ Evid Based Med.* 2018;23(2):60-63.
8. Ansari ZA, Choi CJ, Rong AJ, Erickson BP, Tse DT. Ocular and cerebral infarction from periocular filler injection. *Orbit.* 2019;38(4):322-324.
9. Bitar S, Gomez CR. Stroke following injection of a melted suppository. *Stroke.* 1993;24(5):741-743.
10. Danesh-Meyer HV, Savino PJ, Sergott RC. Case reports and small case series: ocular and cerebral ischemia following facial injection of autologous fat. *Arch Ophthalmol.* 2001;119(5):777-778.
11. Feinendegen DL, Baumgartner RW, Vuadens P, et al. Autologous fat injection for soft tissue augmentation in the face: a safe procedure? *Aesthetic Plast Surg.* 1998;22(3):163-167.
12. He MS, Sheu MM, Huang ZL, Tsai CH, Tsai RK. Sudden bilateral vision loss and brain infarction following cosmetic hyaluronic acid injection. *JAMA Ophthalmol.* 2013;131(9):1234-1235.
13. Hong JH, Ahn SJ, Woo SJ, et al. Central retinal artery occlusion with concomitant ipsilateral cerebral infarction after cosmetic facial injections. *J Neurol Sci.* 2014;346(1-2):310-314.
14. Hong DK, Seo YJ, Lee JH, Im M. Sudden visual loss and multiple cerebral infarction after autologous fat injection into the glabella. *Dermatol Surg.* 2014;40(4):485-487.
15. Hu J, Chen W, Wu Y, et al. Middle cerebral artery occlusion following autologous bitemporal fat injection. *Neurol India.* 2011;59(3):474-475.

16. Huo X, Liu R, Wang Y, et al. Cerebral fat embolism as complication of facial fat graft: retrospective analysis of clinical characteristics, treatment, and prognosis. *World Neurosurg.* 2018;120:249-255.
17. Kang JH, Park KH, Park JS. Acute mental change and hemiplegia after autologous fat injection. *J Cosmet Laser Ther.* 2016;18(7):413-416.
18. Kim SN, Byun DS, Park JH, et al. Panophthalmoplegia and vision loss after cosmetic nasal dorsum injection. *J Clin Neurosci.* 2014;21(4):678-680.
19. Kim EG, Eom TK, Kang SJ. Severe visual loss and cerebral infarction after injection of hyaluronic acid gel. *J Craniofac Surg.* 2014;25(2):684-686.
20. Lee DH, Yang HN, Kim JC, Shyn KH. Sudden unilateral visual loss and brain infarction after autologous fat injection into nasolabial groove. *Br J Ophthalmol.* 1996;80(11):1026-1027.
21. Lee YJ, Kim HJ, Choi KD, Choi HY. MRI restricted diffusion in optic nerve infarction after autologous fat transplantation. *J Neuroophthalmol.* 2010;30(3):216-218.
22. Lee CM, Hong IH, Park SP. Ophthalmic artery obstruction and cerebral infarction following periocular injection of autologous fat. *Korean J Ophthalmol.* 2011;25(5):358-361.
23. Li KT, Huang YH, Chen CH, Chou LW. Delayed-onset cerebral infarction after cosmetic facial injection using hyaluronic acid. *J Formos Med Assoc.* 2016;115(7):587-588.
24. Lin YC, Chen WC, Liao WC, Hsia TC. Central retinal artery occlusion and brain infarctions after nasal filler injection. *QJM* 2015;108(9):731-732.
25. Liu H, Wu X, Zhang X, Niu C, Zhu H. Internal carotid artery embolism after autologous fat injection for temporal augmentation. *Aesthetic Plast Surg.* 2019;43(2):383-387.
26. Liu L, Yin M, Liu S, Hu M, Zhang B. Facial filler causes stroke after development of cerebral fat embolism. *Lancet.* 2020;395(10222):449.
27. Marumo Y, Hiraoka M, Hashimoto M, Ohguro H. Visual impairment by multiple vascular embolization with hydroxyapatite particles. *Orbit.* 2018;37(3):165-170.
28. Park SW, Woo SJ, Park KH, Huh JW, Jung C, Kwon OK. Iatrogenic retinal artery occlusion caused by cosmetic facial filler injections. *Am J Ophthalmol.* 2012;154(4):653-62 e1.
29. Ragam A, Agemy SA, Dave SB, Khorsandi AS, Banik R. Ipsilateral ophthalmic and cerebral infarctions after cosmetic polylactic acid injection into the forehead. *J Neuroophthalmol.* 2017;37(1):77-80.
30. Renard D, Charavel P, Dahmani L, Freitag C. Cerebral fat embolism after autologous fat injection for reconstructive eye surgery. *Rev Neurol (Paris).* 2019;175(1-2):94-95.
31. Roshandel D, Soheilian M, Pakravan M, Aghayan S, Peyman GA. Middle cerebral artery, ophthalmic artery, and multibranch retinal vessel occlusion after cosmetic autologous fat transfer to forehead. *Ophthalmic Surg Lasers Imaging Retina.* 2015;46(5):593-596.
32. Shen X, Li Q, Zhang H. Massive cerebral infarction following facial fat injection. *Aesthetic Plast Surg.* 2016;40(5):801-805.
33. Thaunat O, Thaler F, Loirat P, Decroix JP, Boulin A. Cerebral fat embolism induced by facial fat injection. *Plast Reconstr Surg.* 2004;113(7):2235-2236.
34. Toledano S, Zyss J, Gerber S, Rodallec M, Zuber M. Fat emboli responsible for ischemic stroke in reconstructive eye surgery. *J Neurol.* 2010;257(11):1927-1928.
35. Wang DW, Yin YM, Yao YM. Internal and external carotid artery embolism following facial injection of autologous fat. *Aesthet Surg J.* 2014;34(8):NP83-NP87.
36. Wang X, Wu M, Zhou X, Liu H, Zhang Y, Wang H. Autologous fat used for facial filling can lead to massive cerebral infarction through middle cerebral artery or facial intracranial branches. *J Craniofac Surg.* 2018;29(5):1341-1343.
37. Wang C, Sun T, Zhu L, Zhang Y, Wang X. Emotional disorder syndrome after cosmetic facial injection. *J Cosmet Dermatol.* 2020;19(9):2273-2276.
38. Yoon SS, Chang DI, Chung KC. Acute fatal stroke immediately following autologous fat injection into the face. *Neurology.* 2003;61(8):1151-1152.
39. Zhang L, Luo Z, Li J, et al. Endovascular hyaluronidase application through superselective angiography to rescue blindness caused by hyaluronic acid injection. *Aesthet Surg J.* 2021;41(3):344-355.
40. Zhou K, Cai C. The successful mechanical lipectomy treatment of cerebral fat embolism following autologous fat injection. *Plast Reconstr Surg Glob Open.* 2019;7(1):e2091.
41. Wu WT, Liew S, Chan HH, et al. Consensus on current injectable treatment strategies in the Asian face. *Aesthetic Plast Surg* 2016;40(2):202-214.
42. Taveras JM, Mount LA, Friedenberg RM. Arteriographic demonstration of external-internal carotid anastomosis through the ophthalmic arteries. *Radiology.* 1954;63(4):525-530.
43. Wu WT. The Oriental nose: an anatomical basis for surgery. *Ann Acad Med Singapore.* 1992;21(2):176-189.
44. Zhang L, Pan L, Xu H, et al. Clinical observations and the anatomical basis of blindness after facial hyaluronic acid injection. *Aesthetic Plast Surg.* 2019;43(4):1054-1060.
45. LeSavage BL, Suhar NA, Madl CM, Heilshorn SC. Production of elastin-like protein hydrogels for encapsulation and immunostaining of cells in 3D. *J Vis Exp.* 2018;(135):57739.
46. Jang JG, Hong KS, Choi EY. A case of nonthrombotic pulmonary embolism after facial injection of hyaluronic acid in an illegal cosmetic procedure. *Tuberc Respir Dis (Seoul).* 2014;77(2):90-93.
47. Tansatit T, Apinuntrum P, Phetudom T. An anatomical study of the middle temporal vein and the drainage vascular networks to assess the potential complications and the preventive maneuver during temporal augmentation using both anterograde and retrograde injections. *Aesthetic Plast Surg.* 2015;39(5):791-799.
48. Kapoor KM, Bertossi D, Li CQ, Saputra DI, Heydenrych I, Yavuzer R. A systematic literature review of the middle temporal vein anatomy: “venous danger zone” in

temporal fossa for filler injections. *Aesthetic Plast Surg*. 2020;44(5):1803-1810.
49. Zhang LX, Lai LY, Zhou GW, et al. Evaluation of intraarterial thrombolysis in treatment of cosmetic facial filler-related ophthalmic artery occlusion. *Plast Reconstr Surg*. 2020;145(1):42e-50e.
50. Zhang L, Feng X, Shi H, Wu WTL, Wu S. Blindness after facial filler injections: the role of extravascular hyaluronidase on intravascular hyaluronic acid embolism in the rabbit experimental model. *Aesthet Surg J*. 2020;40(3):319-326.
51. Kumar N, Swift A, Rahman E. Development of "core syllabus" for facial anatomy teaching to aesthetic physicians: a Delphi consensus. *Plast Reconstr Surg Glob Open*. 2018;6(3):e1687.
52. Schelke LW, Decates TS, Velthuis PJ. Ultrasound to improve the safety of hyaluronic acid filler treatments. *J Cosmet Dermatol*. 2018;17(6):1019-1024.
53. Fabi SG, Goldman MP, Mills DC, et al. Combining microfocused ultrasound with botulinum toxin and temporary and semi-permanent dermal fillers: safety and current use. *Dermatol Surg*. 2016;42(Suppl 2):S168-S176.
54. Schelke LW, Velthuis P, Kadouch J, Swift A. Early ultrasound for diagnosis and treatment of vascular adverse events with hyaluronic acid fillers. *J Am Acad Dermatol*. 2019;S0190-9622(19)32392-8.

Aesth Plast Surg (2020) 44:543–548
https://doi.org/10.1007/s00266-019-01589-x

ATTACHMENT D

CASE REPORT NON-SURGICAL AESTHETIC

Fatal Cerebral Infarction and Ophthalmic Artery Occlusion After Nasal Augmentation with Hyaluronic Acid—A Case Report and Review of Literature

Qing Yang[1] · Binglun Lu[2] · Ning Guo[3] · Liang Li[4] · Yanjun Wang[5] · Xianjie Ma[1] · Yingjun Su[1]

Received: 18 September 2019 / Accepted: 7 December 2019 / Published online: 13 January 2020

Abstract

Background Cerebral infarction is a rare complication of hyaluronic acid (HA) filler injection, usually presenting with sudden increase in intracranial pressure and loss of vision.

Methods A 40-year-old Asian woman in a coma was transferred to the emergency intensive care unit of Xijing Hospital, China, 48 h after nasal augmentation with HA. Magnetic resonance imaging indicated cerebral infarction and left optic nerve edema and ischemia. Magnetic resonance angiography did not reveal vessel embolism.

Results The patient developed gastric ulceration, pulmonary infection, respiratory failure, and cerebral herniation, and died 6 days after the HA filler injection.

Conclusion Facial cosmetic HA filler injection can cause devastating and even fatal complications.

Qing Yang and Binglun Lu have contributed equally to this study.

✉ Xianjie Ma
2364205307@qq.com

✉ Yingjun Su
suyingjun@fmmu.edu.cn

[1] Department of Plastic and Reconstructive Surgery, Xijing Hospital, Fourth Military Medical University, No. 127 Changle West Road, Xi'an 710032, Shaanxi, China

[2] Department of Plastic and Reconstructive Surgery, Changan Hospital, Xi'an 710016, Shaanxi, China

[3] Department of Radiology, Xijing Hospital, Fourth Military Medical University, Xi'an 710032, Shaanxi, China

[4] Department of Neurosurgery, Xijing Institute of Clinical Neuroscience, Xijing Hospital, Fourth Military Medical University, Xi'an 710032, Shaanxi, China

[5] Department of Emergency Medicine, Xijing Hospital, Fourth Military Medical University, Xi'an 710032, Shaanxi, China

Level of Evidence V This journal requires that authors assign a level of evidence to each article. For a full description of these Evidence-Based Medicine ratings, please refer to the Table of Contents or the online Instructions to Authors www.springer.com/00266.

Keywords Cerebral infarction · Hyaluronic acid · Embolism

Introduction

Iatrogenic cerebral infarction is a rare complication of hyaluronic acid (HA) injection for cosmetic purposes, mainly occurring after filler injection into the glabellar and nasal regions [1–3]. Sudden loss of vision, altered consciousness, and weakness of limbs during or shortly after the HA filling procedure are generally the first indication of the occurrence of cerebral infarction. Rapidly progressing brain ischemia can lead to irreversible cerebral neuron necrosis and even death. It is important to increase awareness regarding this serious complication, as outcomes could be improved with early diagnosis and appropriate intervention. We report a case of massive cerebral infarction and ophthalmic artery occlusion after HA injection for nasal augmentation. The patient died of cerebral herniation and multiple organ dysfunction syndrome. We discuss the pathogenesis, treatment, and prognosis of this serious syndrome and briefly review the related literature.

This retrospective study was approved by the Institutional Research Ethics Committee of Xijing Hospital (Approval No. KY20192122-C-1), and signed informed consent was obtained from the patient's family representative.

Case Presentation

A 40-year-old Asian woman in a coma was transferred to the emergency intensive care unit of our hospital 48 h after she had undergone nasal augmentation by lidocaine-containing HA injection by an unlicensed practitioner.

She had reportedly received 2 mL lidocaine-containing HA filler injection via a 25G blunt cannula, with topical 5% lidocaine cream applied for local anesthesia about 40 min before HA injection. No other medication was administered during the procedure. Immediately after the HA injection, the patient had complained of periocular pain and blurred vision in the left eye. She developed nausea, vomiting, and headache, and lost consciousness within 30 min. She was taken to the local hospital 4 h post-injection. According to her relatives, she had no history of coagulopathy or other systemic disease; however, 1 week earlier, she had undergone cosmetic facial autologous fat injection at a private plastic surgery clinic, and had light facial edema and ecchymosis when she presented for the HA injection.

On examination at the local hospital, the patient was drowsy, with dilated and nonreactive pupil, blepharoptosis, and absent light reflex in the left eye. The right eye was normal. The skin over the forehead, bilateral periorbital regions, and nasal dorsum showed petechial hemorrhages and purple discoloration. The initial Glasgow Coma Scale (GCS) score was 8, with a positive right Babinski sign and a shallow right nasolabial fold. Diffusion-weighted imaging (DWI; Fig. 1a, b) performed 24 h after the HA injection revealed hyperacute embolic infarction involving the left frontal and parietal lobes, as well as multifocal infarctions in the left temporal and occipital lobes, and the right frontal and temporal lobes. T2-weighted images (Fig. 1c) revealed high signal intensity of the optic nerve in the left eye, indicating edema and ischemia. Magnetic resonance angiography (MRA; Fig. 1d), however, did not show embolisms of the anterior, middle, and posterior cerebral arteries and the circle of Willis and their branches. With a tentative diagnosis of cerebral infarction of undetermined etiology, intravenous mannitol and glucocorticoid were administered to relieve the cerebral edema. However, her condition worsened continuously and was therefore transferred to our hospital.

At admission to our hospital, she had GCS score 4. Physical examination showed the features of persistent intracranial hypertension. Her respiratory rate was six breaths per minute and heart rate 37 beats per minute; blood pressure was 75/43 mmHg. The electrocardiogram showed sinus bradycardia, arrhythmia, and nodal escape. Blood examination revealed hypokalemia and relative hypercoagulability.

She was mechanically ventilated, and administered medications to maintain blood pressure, reduce neuronal damage, and correct electrolyte imbalance. Emergency decompressive craniectomy was advised, but her guardians refused the procedure. She developed gastric ulceration, pulmonary infection, respiratory failure, and cerebral herniation, and died 6 days after the filler injection.

Discussion

There have been several previous reports of cerebral infarction and ophthalmic artery occlusion after HA injections in the facial areas. Seven of these reports (including ours) are summarized in Table 1 [4–9]. Our patient was the only death.

Our patient was initially suspected to have delayed-onset cerebral infarction induced by autologous fat transplantation (performed a week earlier) and a hypercoagulable status. The patient's skin compromise after the HA filler was mild at the early stage, and whether the etiologic causes for the skin edema and ecchymosis were associated with the earlier autologous fat injection was difficult to identify. Delayed cerebral infarction induced by autologous fat transplantation has not been previously reported. And a published case of a patient who suffered from delayed-onset cerebral infarction 9 h after an immediate sudden onset of right eye blindness after HA filler injection for nasal augmentation did not clarify the cause [8]. Our patient demonstrated no eye or nervous system symptoms after the autologous fat injection, and the only sign was local skin edema and ecchymosis 1 week after the injection. Therefore, cerebral autologous fat infarction was ruled out.

The patient MRA result did not show evidence of vessel embolism; moreover, the possibility of cerebral infarction due to a hypercoagulable state was ruled out by the following history and clinical presentation. Firstly, the patient had no history of coagulopathy or cardiovascular disease. Secondly, her left eye blindness and intracranial hypertension occurred within 30 min of HA filler injection. Thirdly, the skin ischemia and necrosis increased rapidly with time (Fig. 2a–c). With no abnormality in the brain MRA results, we speculated that there was probably a rapid distribution of the small HA particles into the capillaries. This possibility is supported by an animal HA-embolus study that found no significant HA emboli in the proximal central artery lumen on histological examination on day 7 after HA injection [10]. Technically, digital subtraction angiography is more sensitive than MRA [11]; however, it could not be performed for our patient because of her unstable clinical condition.

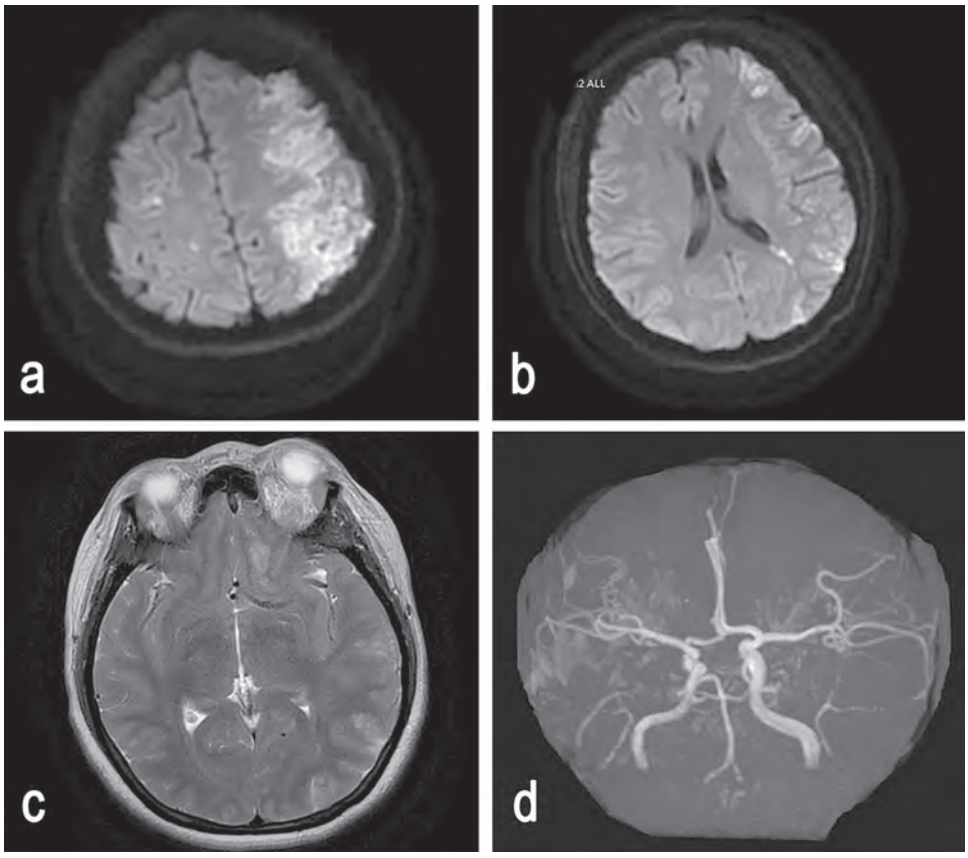


Fig. 1 Magnetic resonance imaging indicates cerebral infarction and left ophthalmic artery occlusion

The rapid progression of HA-derived cerebral embolism may be associated with the hydrophilic nature of HA as such property potentially deteriorates cerebral edema and ischemia. Theoretically, hyaluronidase, urokinase, and other thrombolytic drugs could be effective for HA-derived cerebral embolism in the early stages [12]. Among the seven cases summarized in Table 1, only one patient was treated with intravenous tissue plasminogen activator (tPA) with, however, unsuccessful recanalization of the blocked ophthalmic and cerebral vessels. In contrast, tPA administration caused the intracerebral hemorrhage 24 h later [6]. Intra-arterial thrombolysis and retrobulbar injection of hyaluronidase have been used for HA-induced ophthalmic artery obstruction, but were not very clinically effective because mixed thrombi successively formed after HA entered and blocked the vessels [13]. In animal experiments, intravenous hyaluronidase with urokinase has been successfully used for recanalization of blocked vessels, but the dosage and frequency of application in humans need further study. After cerebral vessel occlusion, there is a 12-h time window before severe function impairment occurs. If there is accompanying optic arterial occlusion, there is a 90-min time window before the ischemia causes irreversible blindness. Thrombolysis should therefore be used without any delay.

Even with optimal medical therapy, malignant cerebral infarction is associated with up to 80% mortality in the first week [14]. Decompressive craniectomy—especially if performed within 48 h—can reduce the risk of mortality and improve functional outcomes in survivors [15]. Unfortunately, that emergency procedure could not be applied to our patient because of the denial of her family.

The supratrochlear, supraorbital, and dorsal nasal arteries are branches of the ophthalmic artery, which arises from the internal carotid artery [16]. In the present case, we speculate that the HA particles were either directly injected or forced into the periorbital arteries, and thence into the ophthalmic artery and cerebral arteries via retrograde blood flow. During HA filler injection, a practical knowledge of the facial vessel anatomy and gentle operation should be taken to minimize trauma. In addition, aspiration before injection can also help to prevent accidental intravascular injection.

The possibility of vessel compromise caused by HA filler injection is thought by some physicians to be lower with blunt cannulas than that with needles, but the risk cannot be completely avoided [17]. During the HA injection procedure, physicians could not sense the cannula tip clearly, and the patient presents with local hypoalgesia due to the effect of lidocaine contained in the HA suspension.

Table 1 Summary of clinical characteristics of our patient and of previously reported cases of cerebral infarction secondary to cosmetic facial HA injection

Author	Year	Age	Sex	Number of cases	Site of HA injection	Dose of HA	Cerebral infarction		Ophthalmic occlusion	Intravenous thrombolysis	Operation	Follow-up
							Site	MRA/CTA (time)				
He MS et al. [4]	2013	52	F	1	Glabella	Absent	R frontal, occipital, and parietal lobes	Absent	R CRA	N	N	R eye blindness and L hemianopia with L eye
Hong JH et al. [5]	2014	50	F	1	Glabella and cheeks	Absent	L anterior and middle cerebral artery territories	Absent	L CRA	N	N	L eye blindness and ptosis, R hemiparesis and facial palsy
Kim EG et al. [6]	2014	23	M	1	Nose	Absent	R frontotemporoparietal lobes	Absent	R OA	tPA*	Decompressive craniectomy	R eye blindness L limb paralysis right facial palsy
Lin, Y-C et al. [7]	2015	25	F	1	Nose	Absent	B middle cerebral artery territories	MRA (< 1 d)	R CRA	Absent	Absent	R eye blindness and ptosis, L upper limb hemiparesis
Li KT [8]	2016	25	F	1	Nose	Absent	R middle cerebral artery territory	Absent	R CRA	Absent	Absent	R eye blindness, and L upper limb hemiparesis
Ansari ZA et al. [9]	2018	20	F	1	R lateral glabella	Absent	B parietal lobes	Absent	R OA	N	N	R eye blindness
Present study		36	F	1	Nose	2 mL	B frontal, temporal and left parietal, occipital lobes	MRA (8 h)	L OA	N	N	Died

R right; *L* left; *B* bilateral; *CRA* central retinal artery; *OA* ophthalmic artery; *tPA* tissue plasminogen activator; *DC* decompressive craniectomy

*The patient had cerebral hemorrhagic transformation after 24 h after thrombolysis with tPA

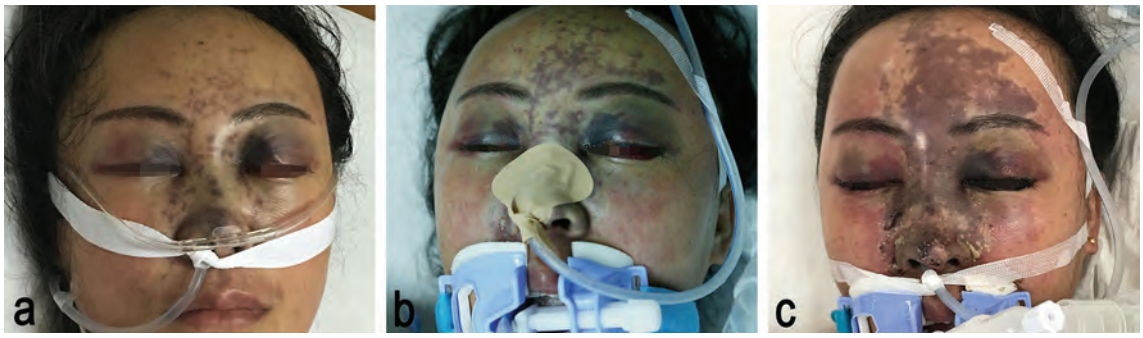


Fig. 2 Skin ischemia and necrosis increased with time. 24 h post-injection (**a**); 3 days post-injection (**b**); 5 days post-injection (**c**)

When vessels were blocked by HA during the procedure, it was hard to be aware of and to be discontinued immediately until the patient complained about periocular pain, blurred vision, and/or began vomiting. Like the case in this study, the patient did not complain until obvious pain or serious complication occurred.

This case clearly demonstrates that the operating personnel who performed lidocaine-containing HA filler injection with blunt cannula cannot entirely avoid vessel compromise. Once this has occurred, the outcome could be devastating. Furthermore, HA injection should be paused if the patient presents with edema and ecchymosis over the local skin area, so as to avoid the uncertainty should ischemia induced by HA embolism occur during the filler injection procedure.

Conclusion

HA filler injection in the facial region may result in devastating and fatal complications. Early diagnosis and timely multidisciplinary consultation may help reduce mortality and improve functional outcomes for survivors. HA injection should be avoided in patients having edema and ecchymosis in the local skin, as that would interfere with the identification of ischemia induced by HA embolism. The operating physician should always keep in mind the complex anatomy of the nasal–ophthalmic–cerebral vessels and the possibility of HA-induced embolism formation.

Compliance with Ethical Standards

Conflict of interest The authors claim no conflict of interest in this study.

Ethical Approval This retrospective study was approved by the Institutional Research Ethics Committee of Xijing Hospital (Approval No. KY20192122-C-1).

Informed Consent Signed informed consent was obtained from the patient's family representative.

References

1. Qin J, Qi X, Zhou J, Wu PS et al (2017) Analysis of artery occlusion caused by facial autologous fat injections. Zhonghua Yan Ke Za Zhi 53(8):594–598
2. Szantyr A, Orski M, Marchewka I, Szuta M et al (2017) Ocular complications following autologous fat injections into facial area: case report of a recovery from visual loss after ophthalmic artery occlusion and a review of the literature. Aesthet Plast Surg 41(3):580–584
3. Sito G, Manzoni V, Sommariva R (2019) Vascular complications after facial filler injection: a literature review and meta-analysis. J Clin Aesthet Dermatol 12(6):E65–E72
4. He MS, Sheu MM, Huang ZL, Tsai CH et al (2013) Sudden bilateral vision loss and brain infarction following cosmetic hyaluronic acid injection. JAMA Ophthalmol 131(9):1234
5. Hong JH, Ahn SJ, Woo SJ, Jung C et al (2014) Central retinal artery occlusion with concomitant ipsilateral cerebral infarction after cosmetic facial injections. J Neurol Sci 346(1–2):310–314
6. Kim EG, Eom TK, Kang SJ (2014) Severe visual loss and cerebral infarction after injection of hyaluronic acid gel. J Craniofac Surg 25(2):684–686
7. Lin YC, Chen WC, Liao WC, Hsia TC et al (2015) Central retinal artery occlusion and brain infarctions after nasal filler injection. QJM 108(9):731–732
8. Li KT, Huang YH, Chen CH, Chou LW (2016) Delayed-onset cerebral infarction after cosmetic facial injection using hyaluronic acid. J Formos Med Assoc 115(7):587–588
9. Ansari ZA, Choi CJ, Rong AJ, Erickson BP et al (2019) Ocular and cerebral infarction from periocular filler injection. Orbit 38(4):322–324
10. Zhuang Y, Yang M, Liu C (2016) An islanded rabbit auricular skin flap model of hyaluronic acid injection-induced embolism. Aesthet Plast Surg 40(3):421–427
11. Yao B, Shen F, Zhao X, Liu G et al (2019) Ophthalmic artery occlusion combined with superior sagittal sinus thrombosis caused by hyaluronic acid injection for facial soft tissue augmentation: a case report. Medicine (Baltimore) 98(36):e17048
12. Park KH, Kim YK, Woo SJ, Kang SW et al (2014) Iatrogenic occlusion of the ophthalmic artery after cosmetic facial filler injections: a national survey by the Korean Retina Society. JAMA Ophthalmol 132(6):714–723
13. Wang M, Li W, Zhang Y, Tian W et al (2017) Comparison of intra-arterial and subcutaneous testicular hyaluronidase injection treatments and the vascular complications of hyaluronic acid filler. Dermatol Surg 43(2):246–254
14. Mohan RK, Crocker M, Moynihan B (2017) Decompressive craniectomy for the treatment of malignant middle cerebral artery infarction. Br J Neurosurg 31(4):401–409

15. Lu X, Huang B, Zheng J, Tao Y et al (2014) Decompressive craniectomy for the treatment of malignant infarction of the middle cerebral artery. Sci Rep 17(4):7070
16. Loh KT, Chua JJ, Lee HM, Lim JT et al (2016) Prevention and management of vision loss relating to facial filler injections. Singapore Med J 57(8):438–443
17. Signorini M, Liew S, Sundaram H, De Boulle KL et al (2016) Global aesthetics consensus: avoidance and management of complications from hyaluronic acid fillers-evidence- and opinion-based review and consensus recommendations. Plast Reconstr Surg 137(6):961e–971e

Original Article

Serious Adverse Events With Injectable Fillers: Retrospective Analysis of 7,659 Patient Outcomes

Jessica A. Kern, BS,* Ramya Kollipara, MD,† Elika Hoss, MD,‡ Monica Boen, MD,§ Douglas C. Wu, MD, PhD,§ William Groff, DO,§ and Mitchel P. Goldman, MD§

BACKGROUND In total, 2.7 million injectable filler treatments were performed in 2019 in the United States. Although generally considered to be a safe treatment modality, adverse events may occur in rare situations.

OBJECTIVE Analyze serious adverse events from injectable filler treatments, including infections, cutaneous necrosis, blindness, or delayed-onset nodule formation, spanning 11 years for 3 board-certified dermatologists and review their incidence, management, and outcomes.

MATERIALS AND METHODS A retrospective analysis was performed of injectable filler treatments spanning 11 years at a multipractitioner outpatient clinic. Serious adverse events were identified, and treatment measures were documented. A literature search was performed to determine recent trends and outcomes for comparison.

RESULTS Between January 2009 and August 2020, 18,013 mL of injectable filler was administered to 7,659 patients. Of the 18,013 mL administered, 74.1% comprised hyaluronic acid derivatives, 19.19% poly-L-lactic acid, and 6.71% calcium hydroxylapatite. Four serious adverse events were identified. Three events were delayed-onset skin nodule formation. One adverse event was related to vascular compromise and subsequent cutaneous necrosis. After appropriate treatment, all adverse events resolved without significant long-term sequelae.

CONCLUSION Serious adverse events associated with injectable fillers, when performed by board-certified dermatologists, are extremely rare and can be successfully managed with appropriate treatment.

In total, 2.7 million injectable filler treatments were performed in 2019 in the United States for indications including volume enhancement and cosmetic improvement of wrinkles.[1] Recent data indicate a steady rise in the number of treatments performed annually, and since 2000, this increase has exceeded 300%.[1–3] As the number of treatments increase, so too has the incidence of serious filler-related adverse events, including cutaneous necrosis, blindness, and delayed-onset nodule formation.[4–6] This study analyzes injectable filler treatments spanning 11 years at a high-volume cosmetic dermatology practice to determine the incidence, management, and final outcome of these filler-related adverse events. The author's also review the literature to evaluate recent trends and outcomes for comparison.

Methods

Injectable filler treatments performed by 3 board-certified dermatologists at a multipractitioner cosmetic dermatology clinic were examined from January 2009 to August 2020. The total amount and type of filler in addition to the number of patients were calculated through review of electronic medical records. Subsequently, any serious adverse event related to infection, vascular compromise with subsequent cutaneous necrosis and/or blindness, or delayed inflammatory reaction was identified. Evaluation, management, and final outcomes of the adverse events were documented. Finally, a literature search was performed to evaluate recent trends in injectable filler outcomes for review and comparison.

Results

In total, 18,013 mL of filler were administered to 7,659 patients. This comes out to an average of 2.3 mL of filler per patient which represents the total volume injected into multiple different areas, such as the cheeks, temples, and lips, all in a single session with never more than 0.5 mL injected into a single site. Fifteen unique formulations were used. Hyaluronic acid derivatives comprised 74.1% (13,348 mL) of the fillers used. This was followed by poly-L-lactic acid at 19.2% (3,457 mL) and calcium hydroxylapatite at 6.7% (1,208 mL). Most of the patients, 82% (6,280), were treated with hyaluronic acid fillers, followed by 12.4% (948) with poly-L-lactic acid and 5.6% (431) with calcium hydroxylapatite.

Four adverse events were identified. Three were delayed nodule formation at the treatment site. The other was related to vascular compromise and secondary cutaneous necrosis (Figure 1). Anatomically, all the cases involved the

*From the *University of California, San Diego School of Medicine, San Diego, California; †Westlake Dermatology and Cosmetic Surgery, Dallas, Texas; ‡Department of Dermatology, Mayo Clinic, Scottsdale, Arizona; §Cosmetic Laser Dermatology, A West Dermatology Company, San Diego, California*

M. P. Goldman has consulted and/or conducted research for Galderma, Merz and Allergan. The remaining authors have indicated no significant interest with commercial supporters.

Address correspondence and reprint requests to: Jessica A. Kern, BS, Cosmetic Laser Dermatology, 9339 Genesee Avenue No 300, San Diego, CA 92122, or e-mail: jkern@health.ucsd.edu

http://dx.doi.org/10.1097/DSS.0000000000003409

cheeks, with 1 case of delayed nodules involving both the cheeks and lips.

All the cases of delayed nodules were attributed to the administration of hyaluronic acid filler alone (0.02% overall incidence per hyaluronic acid syringe), whereas the case of cutaneous necrosis developed after injection of calcium hydroxylapatite filler alone (0.08% incidence per syringe). Of note, the patient who developed cutaneous necrosis had a history of nonabsorbable filler comprised polymethylmethacrylate microspheres in the treatment area 3 years before. Two cases of delayed nodules arose after the treatment with Juvéderm Voluma (0.05% incidence per syringe; Allergan, Dublin, Ireland) and the other case occurred with the use of Juvéderm Volbella (0.20% incidence per syringe; Allergan, Dublin, Ireland). The average time of onset for the delayed nodules was 5.5 months from the most recent injection. One patient was able to recall upper respiratory infection symptoms 1 week before the onset. This same patient was also noted to have fractional CO_2 laser treatment to the perioral area 8 days before the onset of the nodule.

Management of each adverse event varied as presented in Table 1. In the case of cutaneous necrosis, initial treatment consisted of aspirin, pentoxifylline, nitroglycerin paste, 8 minutes of red light therapy to decrease inflammation, and prophylactic clarithromycin and valacyclovir. After noting minimal improvement, the patient was then treated with 14 dives of hyperbaric oxygen therapy. Treatment of the delayed nodules varied and included intralesional hyaluronidase, a combination of intralesional hyaluronidase, triamcinolone, 5-fluorouracil, and intramuscular triamcinolone. Overall, after appropriate treatment was performed, all adverse events resolved without lasting morbidity or mortality.

Discussion

The authors' experience demonstrates a favorable safety profile for injectable fillers when administered by an experienced dermatologist. Serious adverse events, albeit rare, were quickly identified and managed appropriately with no significant long-term sequelae.

Several recent studies have evaluated filler-related complications within the United States and abroad. Three of these studies obtained data from the US FDA's manufacturer and user device experience (MAUDE) database to identify filler-related adverse events during varying periods from 1993 to 2017.

Numerous similarities were identified between the author's findings and those reported in the MAUDE database. The cheeks, followed by the lips, were the most commonly affected anatomical site regardless of the filler type. Hyaluronic acid resulted in the highest number of total adverse events (likely due, in part, to being the most injected filler).[4,7,8] In most of the cases involving more severe complications, namely, vascular compromise, calcium hydroxylapatite was used.[4,7,8] Although the MAUDE database provides the largest compilation of soft tissue complications, many limitations exist including incomplete reporting and the ability for nonhealth care providers to place entries.[4,7,8] Therefore, health care providers should use a level of discernment when using these data to guide treatment decisions.

Vascular occlusion and its potential sequelae continue to be the most feared complication associated with fillers. Occlusion can occur because of direct compromise of the intravascular space, compression of the vessel because of the surrounding edema and mass effect, or embolization of the filler to a distant site.[9] Depending on the anatomical location and percentage of occlusion, sequelae can range from local tissue necrosis to blindness and even stroke.[10] Even with prompt management, vascular complications can be irreversible. Therefore, a thorough understanding of facial anatomy is imperative before the administration of filler. In addition, it is important that patients divulge their cosmetic treatment history before receiving filler because complications can arise because of underlying fibrosis, anatomic variations, or other skin changes resulting from previous procedures. Although aspiration before hyaluronic acid filler injection is a debated safety measure, it is not routinely performed by the authors. After injection, pain and changes in skin color (i.e., blanching, livedo pattern, and delayed capillary refill time) should be observed for

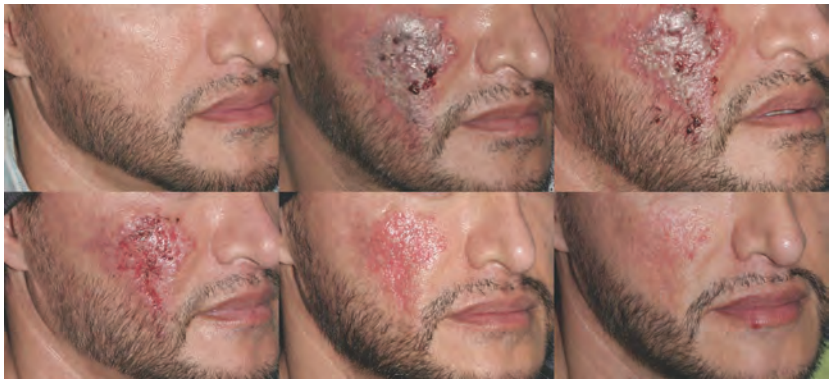


Figure 1. A 34-year-old man with progressive tissue necrosis and subsequent healing after the administration of 1.5 mL of calcium hydroxylapatite filler to the right medial cheek. The patient was treated with hyperbaric oxygen, topical wound care with silicone dressings, and fractionated laser resurfacing and achieved complete resolution of epidermal scaring.

TABLE 1. Summary of Clinical and Treatment Data From 4 Serious Adverse Events (2009–2020)

Patient Number	Type of Complication	Anatomical Location	Filler Class Used	Treatment and Outcome
1	Cutaneous necrosis	Cheek (site of prior polymethylmethacrylate microspheres injection)	Calcium hydroxylapatite	Aspirin, pentoxifylline, nitroglycerin paste, red light therapy, clarithromycin, valacyclovir, and hyperbaric oxygen (14 dives) with complete resolution
2	Delayed-onset nodule	Bilateral cheeks	Hyaluronic acid	Intralesional hyaluronidase, intralesional triamcinolone, and intralesional 5-fluorouracil with complete resolution
3	Delayed-onset nodule	Bilateral cheeks	Hyaluronic acid	Intralesional hyaluronidase with complete resolution
4	Delayed-onset nodule	Bilateral cheeks and lips	Hyaluronic acid	Intramuscular triamcinolone with complete resolution

pending necrosis, and hyaluronidase should be readily available.

Blindness occurs because of occlusion of the central retinal artery and/or the medial and lateral posterior ciliary arteries arising from the ophthalmic artery.[11] High-risk injection sites for this complication include the glabella, nasal region, nasolabial folds, and forehead.[11–16] In the glabella, forehead, and nasal root/dorsum, retrograde travel of filler from the supratrochlear, supraorbital, or dorsal nasal arteries can result in disruption of the retinal blood supply. Similarly, injection of filler at the nasolabial fold and nasal ala/tip can result in blindness because of anastomoses between the angular and lateral nasal arteries with the dorsal nasal artery. Loss of visual acuity and ocular pain are hallmarks of occlusion, and immediate action must be taken as irreversible loss of retinal ganglion cells occurs after 12 to 15 minutes of nonperfusion.[17]

According to the MAUDE database, 56 cases with visual disturbance were reported in the United States from 1993 to 2014.[4] From a global perspective, roughly 170 cases of filler-related blindness have been reported worldwide with a recent most of the cases occurring after hyaluronic filler administration.[15,16] A preponderance of these cases has been reported in Asian countries, particularly Korea, China, Thailand, and Taiwan.[12–14,16] There are limited data to evaluate this trend.[16] Based on the authors' review of the literature, these countries use the same type of injectable fillers as the United States. One explanation for the higher incidence of cases may be due to standards of beauty in Asia. An anterior projection of the forehead, midface, and chin is considered to be attractive, and thus, filler is placed in higher risk areas, including the glabella, nose, malar cheeks, nasolabial folds, and chin.[16,18,19]

Although overall incidence is rare, these occlusion complications are frequently discussed by the members of the national and international media, and this likely overstates the prevalence to the general public.[20] Estimates of cutaneous necrosis have varied from 1:100,000 to, more recently, 1:10,000 which is stated to be due in part to injection by inexperienced providers.[21,22] However, the author's clinic with an "experienced" injector shows a similar incidence (1:7,659), suggesting that this adverse reaction can occur to anyone. According to the MAUDE database, 121 cases of intra-arterial occlusion with cutaneous necrosis occurred between 2014 and 2016 in the United States.[8]

The incidence of vascular occlusion may also be inflated due to the misdiagnosis of venous congestion as imminent tissue necrosis after an arterial injection. Whereas arterial occlusion is associated with immediate, severe, and disproportionate pain and acute blanching, venous occlusion typically presents later (often once the patient has already left the clinic) with less severe, dull, or even absent pain and dark red/blue discoloration of the skin.[9] In the authors' experience, venous congestion poses minimal risk and can resolve without treatment. A patient seen in the investigators' clinic developed livedo reticularis 3 days after the injection of hyaluronic filler into the nasolabial fold (Figure 2A). His condition was likely due to venous congestion secondary to external compression. A 595-nm pulse dye laser was used at subpurpuric settings to treat the erythema with complete resolution and no scarring or cutaneous compromise (Figure 2B). No hyaluronidase or other treatment was used.

Delayed-onset nodules are a clinically apparent delayed inflammatory reaction in the context of filler administration. Multiple etiologies have been proposed including an underlying infectious process, laboratory contamination during the manufacturing process, and true Type IV hypersensitivity reaction.[23–27] A recent study has classified nodule formation as either an intermediate or late hypersensitivity reaction, appearing 1 week to 1 month, or 1 month to years after injection, respectively, corresponding to the underlying pathophysiology.[28] In addition,

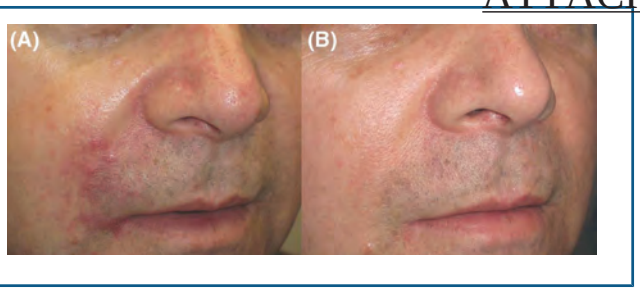


Figure 2. A 50-year-old man 3 days (A) after the injection of hyaluronic acid filler into the nasolabial fold with the onset of livedo reticularis. (A) A 595-nm pulse dye laser was used at subpurpuric settings to treat the erythema. At the 7-month follow-up (B), there was complete resolution and no scaring or clinical evidence of cutaneous compromise. No hyaluronidase was used. The cause was most likely venous congestion secondary to external compression by the hyaluronic filler.

numerous authors have proposed that products containing Vycross technology (Juvéderm Voluma, Volbella, Volift, or Retouch) have higher incidence rates because of the combination of both high and low molecular weight hyaluronic acid chains and the latter's ability to directly activate the immune system.[23–26] A recent systematic review of FDA-approved hyaluronic acid fillers determined an incidence of 1.1% per year after pooling the data from 35 prospective studies. Furthermore, 7 retrospective studies were analyzed, and although 2 were noted to have major flaws, the overall estimated percentage of delayed inflammatory reactions was <1% in 1 to 5.5 years.[27] Another large retrospective review determined the incidence of these lesions at 0.98% per patient, 0.47% per treatment, and 0.23% per syringe of Juvéderm Voluma. The authors note that the lesions had a median onset of 4 months after treatment and there was a discernible immunologic stimulus in 34% of the cases.[23] The treatment protocol for delayed-onset nodule formation because of hyaluronic acid filler administration can be directed by the clinical presentation and/or suspected type of nodule etiology—noninflammatory lesions, single/multiple inflammatory lesions, suspected or confirmed granuloma(s), or suspected delayed hypersensitivity reaction.[29] Convery and colleagues [29] present an algorithm to guide treatment based on these features.

Several real-life considerations should be kept in mind when conceptualizing the authors' findings. Numerous studies, including the authors' study, demonstrate favorable safety outcomes when injectable fillers are administered by experienced board-certified dermatologists. A recent study found that board-certified dermatologists injecting fillers for more than 5 years had 70.7% lower odds of vascular occlusion compared with those with less experience.[30] However, there is likely significant underreporting of adverse events by providers from different backgrounds and practice settings. This is supported by a recent survey-based study of 306 American Society of Dermatologic Surgery (ASDS) members which determined that injectable filler treatment resulted in the highest number of complications in patients who visited medical spas.[31] Improper training and technique were cited as the top reasons these complications may have occurred.

The increasing prevalence of illegal and counterfeit fillers should also be considered because a recent study demonstrated a higher incidence of adverse events, including vascular compromise, when treatment was administered by novice injectors and unlicensed practitioners who used non–FDA-approved fillers.[32] Owing to the ease of purchasing counterfeit and/or non–FDA-approved fillers online, in addition to the increasing prevalence of "do it yourself" forums and support groups, the incidence of these adverse events will likely continue to rise.[33,34]

There are limitations of this study to note. One limitation is that only serious adverse events related to infection, vascular compromise with subsequent cutaneous necrosis and/or blindness, or delayed inflammatory reactions were identified and investigated. Minor complications including injection site swelling, erythema, tenderness, and bruising were almost certainly experienced by patients examined in this study but excluded from analysis. Another limitation, by nature of being a chart review, is that the data relied on patients reporting adverse events to their dermatologist and documentation of these reports in their charts. As a result, the authors suspect that there were adverse events not captured in this study. However, the authors believe that most of the events not reported by patients were mild and self-limiting.

In the context of the author' findings and literature review, the authors believe injectable fillers are safe and effective in experienced hands. According to a recent consumer survey published by the ASDS, dermatologists are considered to be the physician of choice for administration of soft tissue fillers, and they were ranked as the top influencer on decisions related to cosmetic procedures.[35] Therefore, it is the author's responsibility to continue educating their patients on the risks, benefits, and safety considerations of this increasingly popular treatment modality.

Acknowledgments

The authors appreciate the tabulation of results by Dr. Ravi Patel.

References

1. American Society of Plastic Surgeons. *Plastic Surgery Statistics Report*; 2019. Available from: https://www.plasticsurgery.org/documents/News/Statistics/2019/plastic-surgery-statistics-full-report-2019.pdf. Accessed September 12, 2020.
2. American Society of Plastic Surgeons. *Plastic Surgery Statistics Report*; 2018. Available from: https://www.plasticsurgery.org/documents/News/Statistics/2018/plastic-surgery-statistics-full-report-2018.pdf. Accessed September 12, 2020.
3. American Society of Plastic Surgeons. *Plastic Surgery Statistics Report*; 2017. Available from: https://www.plasticsurgery.org/documents/News/Statistics/2017/plastic-surgery-statistics-full-report-2017.pdf. Accessed September 12, 2020.

4. Ortiz AE, Ahluwalia J, Song SS, Avram MM. Analysis of U.S. Food and Drug Administration data on soft-tissue filler complications. *Dermatol Surg* 2020;46:958–61.
5. Daines SM, Williams EF. Complications associated with injectable soft-tissue fillers: a 5-year retrospective review. *JAMA Facial Plast Surg* 2013;15:226–31.
6. Scheuer JF, Sieber DA, Pezeshk RA, Campbell CF, et al. Anatomy of the facial danger zones: maximizing safety during soft-tissue filler injections. *Plast Reconstr Surg* 2017;139:50e–58e.
7. Rayess HM, Svider PF, Hanba C, Patel VS, et al. A cross-sectional analysis of adverse events and litigation for injectable fillers. *JAMA Facial Plast Surg* 2018;20:207–14.
8. Beauvais D, Ferneini EM. Complications and litigation associated with injectable facial fillers: a cross-sectional study. *J Oral Maxillofac Surg* 2020;78:133–40.
9. King M, Walker L, Convery C, Davies E. Management of a vascular occlusion associated with cosmetic injections. *J Clin Aesthet Dermatol* 2020;13:E53–E58.
10. Moore RM, Mueller MA, Hu AC, Evans GR. Asymptomatic stroke after hyaluronic acid filler injection: case report and literature review. *Aesthet Surg J* 2021;41:NP602–NP608.
11. Cotofana S, Lachman N. Arteries of the face and their relevance for minimally invasive facial procedures: an anatomical review. *Plast Reconstr Surg* 2019;143:416–26.
12. Sito G, Manzoni V, Sommariva R. Vascular complications after facial filler injection: a literature review and meta-analysis. *J Clin Aesthet Dermatol* 2019;12:E65–E72.
13. Kapoor KM, Kapoor P, Heydenrych I, Bertossi D. Vision loss associated with hyaluronic acid fillers: a systematic review of literature. *Aesthet Plast Surg* 2020;44:929–44.
14. Lee W, Koh IS, Oh W, Yang EJ. Ocular complications of soft tissue filler injections: a review of literature. *J Cosmet Dermatol* 2020;19:772–81.
15. Sorensen EP, Council ML. Update in soft-tissue filler-associated blindness. *Dermatol Surg* 2020;46:671–7.
16. Beleznay K, Carruthers JDA, Humphrey S, Carruthers A, et al. Update on avoiding and treating blindness from fillers: a recent review of the world literature. *Aesthet Surg J* 2019;39:662–74.
17. Tobalem S, Schutz JS, Chronopoulos A. Central retinal artery occlusion—rethinking retinal survival time. *BMC Ophthalmol* 2018;18:101.
18. Bae JM, Lee DW. Three-dimensional remodeling of Young Asian women's faces using 20-mg/ml smooth, highly cohesive, viscous hyaluronic acid fillers: a retrospective study of 320 patients. *Dermatol Surg* 2013;39:1370–5.
19. Donofrio LM. Panfacial volume restoration with fat. *Dermatol Surg* 2005;31:1496–505.
20. Hojjat H, Raad R, Lucas J, Mir M, et al. Public perception of facial fillers. *Facial Plast Surg* 2019;35:204–9.
21. Narins RS, Jewell M, Rubin M, Cohen J, et al. Clinical conference: management of rare events following dermal fillers—focal necrosis and angry red bumps. *Dermatol Surg* 2006;32:426–34.
22. van Loghem J, Funt D, Pavicic T, Goldie K, et al. Managing intravascular complications following treatment with calcium hydroxylapatite: an expert consensus. *J Cosmet Dermatol* 2020;19:2845–58.
23. Humphrey S, Jones DH, Carruthers JD, Carruthers A, et al. Retrospective review of delayed adverse events secondary to treatment with a smooth, cohesive 20-mg/mL hyaluronic acid filler in 4500 patients. *J Am Acad Dermatol* 2020;83:86–95.
24. Goodman GJ. An interesting reaction to a high- and low-molecular weight combination hyaluronic acid. *Dermatol Surg* 2015;41(Suppl 1):S164–6.
25. Artzi O, Cohen JL, Dover JS, Suwanchinda A, et al. Delayed inflammatory reactions to hyaluronic acid fillers: a literature review and proposed treatment algorithm. *Clin Cosmet Investig Dermatol* 2020;13:371–8.
26. Sadeghpour M, Quatrano NA, Bonati LM, Arndt KA, et al. Delayed-onset nodules to differentially crosslinked hyaluronic acids: comparative incidence and risk assessment. *Dermatol Surg* 2019;45:1085–94.
27. Chung KL, Convery C, Ejikeme I, Ghanem AM. A systematic review of the literature of delayed inflammatory reactions after hyaluronic acid filler injection to estimate the incidence of delayed type hypersensitivity reaction. *Aesthet Surg J* 2020;40:NP286–NP300.
28. Mikkilineni R, Wipf A, Farah R, Sadick N. New classification schemata of hypersensitivity adverse effects after hyaluronic acid injections: pathophysiology, treatment algorithm, and prevention. *Dermatol Surg* 2020;46:1404–9.
29. Convery C, Davies E, Murray G, Walker L. Delayed-onset nodules (DONs) and considering their treatment following use of hyaluronic acid (HA) fillers. *J Clin Aesthet Dermatol* 2021;14:E59–E67.
30. Alam M, Kakar R, Dover JS, Harikumar V, et al. Rates of vascular occlusion associated with using needles vs cannulas for filler injection. *JAMA Dermatol* 2021;157:174–80.
31. Wang JV, Albornoz CA, Goldbach H, Mesinkovska N, et al. Experiences with medical spas and associated complications: a survey of aesthetic practitioners. *Dermatol Surg* 2020;46:1543–8.
32. Chayangsu O, Wanitphakdeedecha R, Pattanaprichakul P, Hidajat IJ, et al. Legal vs. illegal injectable fillers: the adverse effects comparison study. *J Cosmet Dermatol* 2020;19:1580–6.
33. Pickett A. Serious issues relating to counterfeit dermal fillers available from Internet sources. *J Am Acad Dermatol* 2011;65:642–3.
34. Brennan R, Wells JS, Van Hout M. "Saving face": an online study of the injecting use of DIY botox and dermal filler kits. *Plast Surg* 2018;26:154–9.
35. American Society for Dermatologic Surgeons. *ASDS Consumer Survey on Cosmetic Dermatologic Procedures*; 2019. Available from: https://www.asds.net/Portals/0/Misc/consumer-survey-2019-powerpoint.pptx. Accessed September 12, 2020.

ATTACHMENT D

Mehta *et al. Plast Aesthet Res* 2022;9:57
DOI: 10.20517/2347-9264.2022.19

Plastic and Aesthetic Research

Review

Open Access

Ischemic complications of dermal fillers

Preeya Mehta[1], Julie Bass Kaplan[2], Sandy Zhang-Nunes[3]

[1]Keck School of Medicine, University of Southern California, Los Angeles, CA 90033, USA.
[2]Disappearing Act Medical Aesthetics, Redding, CA 96001, USA.
[3]Department of Ophthalmology, Roski Eye Institute, University of Southern California, Los Angeles, CA 90033, USA.

Correspondence to: Dr. Sandy Zhang-Nunes, Department of Ophthalmology, Roski Eye Institute, University of Southern California, Los Angeles, CA 90033, USA. E-mail: Sandy.Zhang-Nunes@med.usc.edu

How to cite this article: Mehta P, Kaplan JB, Zhang-Nunes S. Ischemic complications of dermal fillers. *Plast Aesthet Res* 2022;9:57. https://dx.doi.org/10.20517/2347-9264.2022.19

Received: 1 Mar 2022 **First Decision:** 23 May 2022 **Revised:** 26 Jul 2022 **Accepted:** 15 Aug 2022 **Published:** 8 Oct 2022

Academic Editors: Xiaoming Sun, Rona Silkiss **Copy Editor:** Peng-Juan Wen **Production Editor:** Peng-Juan Wen

Abstract

Dermal fillers have become increasingly popular as a cosmetic treatment for facial rejuvenation. Although these injections are generally considered to be safe, as the number of injections has increased, so has the rate of complications. Ischemic complications of fillers include vision loss, ophthalmoplegia, skin necrosis, and cerebral infarction. Knowing the anatomy well is critical to optimally prevent and manage these serious complications. Prevention includes knowledge of the vascular anatomy of the facial area, as well as certain injection techniques such as aspiration, use of a smaller needle, and adoption of a larger cannula. The use of ultrasound has been a recent innovation in preventing and treating filler complications as well. The reversibility of fillers should also be considered when choosing a filler. Some hyaluronic acid (HA) fillers, including the newer ones on the market, are difficult to reverse and non-HA fillers and fat are irreversible. This review aims to discuss facial anatomy, the various ischemic filler complications, the prevention and management of these complications, and the relatively recent use of imaging as an adjunct.

Keywords: Filler complications, soft tissue necrosis, blindness, ophthalmoplegia, cerebral infarction, ischemic complications

INTRODUCTION

Dermal fillers are used to treat changes commonly seen with aging in the face. Since bovine collagen became

FDA approved for cosmetic use in 1981, soft tissue fillers have consistently increased in popularity, with the number of procedures increasing by 50% from 2015 to 2019[1,2]. With this increase in filler injections, there has been a significant increase in the number of products available on the market, with each filler having its own intrinsic properties[3]. While filler injections are generally considered to be a safe procedure, there are still many complications that have been documented and studied in the literature.

The most devastating filler complications are ischemic, which include irreversible vision loss, ophthalmoplegia, and skin necrosis, among other serious complications[4-6]. The incidence of vascular occlusion appears to be up to 3 in 1000 injections[7], and a total of at least 190 cases of blindness have been reported in literature as reviewed by Chatrath *et al*. as of 2019[8]. As of January 2022, we have found at least 211 cases, with Table 1 noting some of the more recent cases. Some cases, like a report of bilateral blindness after nasal augmentation with calcium hydroxylapatite[9], were found to have been missed in previous reviews. Many more cases of blindness have likely gone unreported, so the true incidence is unknown. While the reported cases appear to be a small percentage of the total injections, the rate of this complication appears to be increasing[10,11]. Although the incidence of these complications is low, their severity warrants further studies into how to improve management and prevent these complications from occurring.

This literature review aims to discuss the various ischemic complications seen after injection and their management. Articles until January 2022 were included with a specific focus on recently published literature. This review focuses on the anatomy of the face and ischemic complications seen after filler injections, discusses the management of these complications, reviews prevention techniques, and examines the relatively recent use of imaging as an adjunct.

ANATOMY

The anatomy of the face is complex and has a considerable amount of variation. During a glabellar injection, the supratrochlear and supraorbital arteries are at the highest risk[12]. Both of these arteries supply the superomedial aspects of the forehead and provide retrograde flow to the ophthalmic artery [Figure 1][12,13]. Thus, deep injection is not recommended in this area. However, if the patient understands the risk of injecting in this area and wishes to proceed with this option, an injection with a low G' filler intradermally with the needle still visible may be considered[12]. For forehead augmentation, an intermediate G' filler may also be considered, although the forehead is also a more high-risk area for blindness and ischemia[12].

The facial artery continues midface as the angular artery immediately subjacent to the nasolabial fold [Figure 1][15]. Afterwards, the artery continues towards the nose, where anastomotic vessels join the internal and external carotid territories[15]. In a study that evaluated the facial and angular artery with doppler ultrasound, the authors emphasize that the anatomic variability of the facial artery and angular artery makes it difficult to truly avoid the vasculature in the nasolabial fold area[16]. Given the popularity of treating the nasolabial area, the facial and angular artery in this area are often affected[15]. Therefore, injecting fillers with sharp, fine needles, especially in the region deep to the orbicularis oris or zygomaticus muscle in the nasolabial fold region, may be considered high risk[15]. A recent study found that the most frequent location with a positive blood aspiration was the subperiosteal plane of the pyriform fossa, closely followed by the deep midfacial fat compartments[17]. Additionally, in the nasolabial fold and nasal dorsum areas, the facial, angular, and lateral nasal arteries anastomose with the dorsal nasal artery, a branch of the ophthalmic artery[13]. These arterial anastomoses are a frequent cause of ophthalmic blindness[13]. For deeper volumization in this area, a higher G' filler with a cannula is recommended[12].

ATTACHMENT D

Table 1. Recent case reports of vision loss following filler injections

Author	Demographics	Material	Site of injection	Eye	Symptoms	Time to treatment onset	Treatment	Outcome
Davidova *et al.* (2022)[117]	43-year-old female	Hyaluronic acid	Glabella	Left	Left sided vision loss (NLP) Ptosis Ophthalmoplegia Swelling on left forehead and upper lid Left RAPD	1 h	Ocular massage Aspirin Tinzaparin sodium Methylprednisolone Antiseptic compresses Three hyaluronidase injections in the injection area	Vision remained at NLP at 6 weeks Redness and surface irregularity on the forehead and madarosis on the inner third of the upper lid Restricted EOM at 6 week follow up
Wu *et al.* (2021)[55]	49-year-old female	Poly-L-Lactic acid	Temporal region	Right	Right sided central visual defect Ocular pain Dizziness Nausea Photopsia Right RAPD	1 h	Ocular massage Topical brimonidine Hyperbaric oxygen therapy twice daily for 5 days Dual-antiplatelet treatment (from prior)	Vision remained at NLP in the right eye at 1 year
Danks *et al.* (2021)[118]	38-year-old female	Hyaluronic acid	Right side of nose	Right	Right sided visual loss (NLP) Right sided headache Skin pallor Right RAPD	1) Immediately post injection 2) 4 h after injection	1) 675 IU hyaluronidase to the filler site 2) 3 injections of 1500 IU hyaluronidase; one peribulbar and 2 extraorbital Unknown dose aspirin	Vision improved from NLP to CF at 4 h and 20/20 at 1 month follow up Resolution of right RAPD
Nguyen *et al.* (2021)[119]	27-year-old female	Hyaluronic acid	Nasal dorsum	Right	1) Right sided vision loss (NLP) Right sided ptosis Right sided ophthalmoplegia Frontal and nasal ecchymosis Headache Pain 2) 13 h later, patient developed a headache with ocular pain Right sided vision loss worsened from CF at 1 meter to NLP	4 h	1) 1500 IU hyaluronidase to frontal and nasal areas; 750 IU hyaluronidase retrobulbar; 1500 IU intra-arterial hyaluronidase into the right ophthalmic artery 2) Alteplase 8 mg 1500 IU hyaluronidase Heparin 5000 IU/day Aspirin Nitroglycerin patches Corticosteroid Antibiotic therapy	1) Vision improved from NLP to CF at 1 meter 2) Visual acuity improved from NLP to 20/50 at 3 months Skin ecchymosis fully recovered at 3 months Ophthalmoplegia and eyelid ptosis recovered at 3 months
Lee *et al.* (2021)[102]	39-year-old female	Hyaluronic acid	Glabella	Left	Left sided vision loss (NLP) Left sided ocular pain Drowsy mental status Motor weakness in right upper and lower limbs Dysarthria, hypesthesia, right	Unknown	Methylprednisolone 1 g for 5 days	Vision remained at NLP at 6 weeks Ophthalmoplegia and ptosis partially recovered at 6 weeks

ATTACHMENT D

Mehta *et al. Plast Aesthet Res* 2022;9:57 | https://dx.doi.org/10.20517/2347-9264.2022.19

					arm dominant quadriparesis Left sided ophthalmoplegia and ptosis			
Moore *et al.* (2021)[120]	59-year-old female	Hyaluronic acid	Glabella; nasal dorsum	Right	Right sided vision loss (NLP) Dizziness Nausea Right frontal headache Right RAPD Subclinical punctate strokes Right forehead livedo reticularis	Unknown	Unknown volume hyaluronidase at unknown location 1100 IU retrobulbar hyaluronidase Ocular massage 250 IU of hyaluronidase in glabella and right forehead Warm compresses Topical Nitroglycerin 2% ointment 650 mg aspirin	Vision remained at NLP at 1 week follow up Right forehead had a 1 × 2 cm eschar at 1 week follow up
Eldweik (2021)[121]	32-year-old female	Hyaluronic acid	Nasal bridge	Left	Left sided vision loss (NLP) Swelling and tenderness around left eye Bluish discoloration of facial skin Dull, aching pain Limited EOM Ophthalmoplegia Left blepharoptosis	1) Immediately post injection 2) Less than 1 h	1) 40 IU hyaluronidase at site of injection 2) 300 IU peribulbar injection of hyaluronidase Methylprednisolone 1 g for 5 days Aspirin Antibiotic coverage Antibiotic cream	Vision remained at NLP at 8 weeks Skin necrosis resolved with scarring at 8 weeks Left EOM and blepharoptosis improved at 8 weeks
Jolly *et al.* (2021)[122]	29-year-old female	Unknown	Nasal bridge to tip	Left	Left sided vision loss (LP) only in upper temporal quadrant Left RAPD Left sided ptosis Left sided ophthalmoplegia Reduced EOM Left periorbital ecchymosis Left subconjunctival hemorrhage	6 h	Iopidine 1% 10 min ocular massage 1500 IU hyaluronidase sub-Tenon's injection Anterior chamber paracentesis 250 mg oral acetazolamide	Vision worsened from LP to NLP at 3 months Improvement in EOM and ptosis at 3 months
Hung *et al.* (2021)[54]	31-year-old female	Hyaluronic acid	Nasal dorsum	Right	Right sided vision loss (NLP) Severe sharp pain in retro-orbital area	1) Immediately after injection 2) Unknown	1) Unknown dose of hyaluronidase in treated area 2) 300 mL mannitol intravenously High-flow O_2 3 cycles of ocular massage for 10 s every 4 h 0.15% topical brimonidine 3x daily 250 mg oral acetazolamide 4x daily Aspirin daily 250 mg intravenous methylprednisolone q6h HBOT 2.5 ATA for 90 min daily for 3 weeks	Vision remained at NLP at 5 months Superficial skin necrosis development at 2-week over nasion and rhinion which later resolved at 4-month follow up
Zhang *et al.* (2021)[123]	61-year-old female	Hyaluronic acid	Radix nasi	Right	Right sided severe blurred vision Right sided ptosis	22 h	Glucocorticoids Mannitol Right anterior chamber puncture	Vision remained at NLP at 8 months

					Right sided ophthalmoplegia Swelling in right eye Pain in right eye Nausea Vomiting Chest tightness		Nutritional nerve therapy Endovascular hyaluronidase application through angiography*	
Zhang *et al.* (2021)[123]	31-year-old female	Hyaluronic acid	Glabella and Forehead	Right	Right sided vision loss Ophthalmoplegia Headache Eye pain Chest tightness Nausea Vomiting Sluggishness	30 min	Unknown hyaluronidase dose at the site of injection IV infusion of mannitol Endovascular hyaluronidase application through angiography*	Vision improved from NLP to slight light sensation at 8 months
Zhang *et al.* (2021)[123]	31-year-old female	Hyaluronic acid	Apex nasi	Left	Left sided vision impairment Ptosis Local nose skin pallor Nausea Vomiting Incontinence	4.5 h	Subcutaneous injection of hyaluronidase IV infusion of mannitol Endovascular hyaluronidase application through angiography*	Vision remained at NLP at 3 months
Zhang *et al.* (2021)[123]	46-year-old female	Hyaluronic acid	Palpebra superior	Right	Right sided immediate vision loss Sharp pain at injection site Ptosis	4 h	Subcutaneous hyaluronidase Sublingual administration of nitroglycerin Endovascular hyaluronidase application through angiography*	Vision remained at NLP at 3 months
Liu *et al.* (2020)[124]	29-year-old female	Autologous fat	Forehead	Left	Left sided vision loss (NLP) Ocular pain Left RAPD Decreased IOP Nausea Vomiting Numbness and weakness of right limbs (Grade 2-3) with parietal lobe hyperintense lesion	Immediately after injection	IV infusion of dextran glucose with dexamethasone and mannitol	Vision remained at NLP at 3 months
Liu *et al.* (2020)[124]	46-year-old female	Autologous fat	Forehead	Left	Left sided vision loss (NLP) Ocular pain Nausea Vomiting Decreased IOP Congestion and swelling of injection site Left exotropia (10 degrees) Limited EOM	Immediately after injection	IV infusion of dexamethasone and energy mixture	Vision remained at NLP at 3 months
Liu *et al.* (2020)[124]	38-year-old female	Autologous fat	Forehead	Left	Left sided vision loss (NLP) Ocular pain Nausea	Immediately after injection	IV infusion of dexamethasone and cold compression	Vision remained at NLP at 3 months

ATTACHMENT D

Mehta *et al. Plast Aesthet Res* 2022;9:57 | https://dx.doi.org/10.20517/2347-9264.2022.19

					Vomiting Left RAPD Decreased IOP			Chromatosis at 3 months in the left forehead skin
Conovaloff *et al.* (2020)[125]	59-year-old female	Hyaluronic acid	Supraorbital region	Right	Right sided vision loss (NLP) Dizziness Nausea Frontal headache Right RAPD Punctate infarcts in right frontal and occipital lobes	1) Immediately after injection 2) 120 min	1) Hyaluronidase injection to affected area 2) Nitroglycerin paste Warm compress Eye massage Aspirin 325 mg	Vision remained at NLP at 2 months
Karam *et al.* (2020)[43]	61-year-old female	Platelet-rich plasma	Glabella	Left	1) Left sided vision loss (NLP) Dizziness Vomiting Glabellar bruising Hypoaesthesia in distribution of first trigeminal branch on left side 2) 1 month later, ulceration and skin necrosis in injection area	Unknown	Unknown	Pale left optic disc with pigment, pigmentation of peripheral retina and macular fibrosis at 1 month Retinal detachment in left eye at 8 months Persistent scarring in the injection area at 8 months
Karam *et al.* (2020)[43]	63-year-old female	Platelet-rich plasma	Forehead	Right	Right sided vision loss Dizziness Tinnitus Vomiting Iris depigmentation	Unknown	Unknown	Vision was NLP at 3-week visit
Karam *et al.* (2020)[43]	52-year-old female	Platelet-rich plasma	Nasolabial fold Glabella	Right	Right sided vision loss Pain Incomplete oculomotor nerve palsy Low intraocular pressure	Unknown	Unknown	Vision was NLP at 24 h Necrosis of forehead, right periorbital region, right cheek, and right nasal area at 1 month
Karam *et al.* (2020)[43]	50-year-old female	Platelet-rich plasma Platelet gel injection	Forehead Glabella Right external canthus	Right	Right sided vision loss Transient blue vision preceding loss of vision Headache Nausea Ptosis Urinary urgency	Unknown	Unknown	Vision was NLP at 3 weeks along with complete right oculomotor nerve palsy
Wibowo *et al.* (2019)[62]	40-year-old female	Hyaluronic acid	Nasal dorsum	Right	Right sided blurring of vision (LP) Right sided eyelid ptosis Periorbital swelling, chemosis, conjunctival congestion Discoloration and pustules of nose tip, nose bridge, columella, glabella, forehead,	1) Immediately after injection 2) 3 days	1) Local massage 30 IU of hyaluronidase at unknown location 2) 1500 IU Hyaluronidase in the ischemic zone (5 doses) Aspirin Antibiotics	Improvement in eyelid ptosis at 3 weeks Vision fully recovered from LP at 3 months Minimal skin deformity at 3 months

ATTACHMENT D

					and bilateral medial cheeks Right sided pain		900 IU Hyaluronidase retrobulbar (2 doses)	
Vu *et al.* (2018)[25]	51-year-old female	Calcium Hydroxyapatite	Glabella Dorsum of the nose	Right	Right sided vision loss (NLP) Skin discoloration of right forehead, glabella, dorsum of the nose to nasal tip, medial cheek Nausea Vomiting Headache Right RAPD	12 h	1200 IU retrobulbar injections as 3 serial bolus injections Ocular massage initiated Oral prednisone 60 mg for 3 days 150 IU/day hyaluronidase for skin ischemia Nitroglycerin paste applied to skin Oral aspirin daily Hyperbaric oxygen therapy for skin necrosis	Vision improved from NLP to LP at 3 month follow up Glabella and forehead had erythematous, depressed scars at 3 months
Ramesh *et al.* (2018)[126]	23-year-old male	Hyaluronic acid	Nasal dorsum	Right	1) Right sided vision loss (NLP) Cold sensation in his face and brow Drooping of the right upper eyelid Pustular skin lesions across brow, nose, and face Eye pain 2 days after infection 2) Right sided vision loss (NLP) Retrobulbar ache Reduced EOM Edematous and ptotic eyelid Conjunctival injection and subconjunctival hemorrhage Anterior chamber hypopyon Reduced IOP (8 mm Hg) 1 mm proptosis with resistance to retropulsion Fixed dilated pupil Decreased right V1 sensation Crusted lesions on forehead and nose	1) Unknown time 2) 7 days	1) IV steroids Ocular massage Antibiotics 2) 1200 IU hyaluronidase injected into the orbital apex 600 IU injected into the skin lesions	Vision remained at NLP at 21 days Improvement in ptosis and EOM at 21 days
Chen *et al.* (2018)[127]	31-year-old female	Hyaluronic acid	Right front and eyebrow	Right	Right sided vision loss (NLP) Ocular pain Ophthalmoplegia Ptosis Limited EOM Chills Fatigue Nausea Dizziness	1) Immediate hyaluronidase injection 2) 24 h to thrombolytic therapy 3) 6 days to rest of treatment	1) Unknown injection of hyaluronidase in forehead and eyebrow Unknown dosage of retrobulbar anisodamine Anterior chamber puncture 2) Thrombolytic therapy of urokindase 3) 750 IU hyaluronidase peribulbar/retrobulbar for 5 days	Vision remained at NLP at 3 months Complete recovery in ptosis and EOM at 3 months
Ansari *et al.* (2018)[101]	20-year-old	Hyaluronic acid	Glabella	Right	Right sided vision loss (NLP)	Unknown; patient	Aspirin 325 mg	Unknown

	female				Infarcts of parietal lobes Violaceous pigmentation on the tip and right ala of her nose	came to clinic for 2nd opinion	Prednisone taper	
Kalyam *et al.* (2017)[128]	49-year-old female	Platelet-rich Plasma (PRP)	Forehead rhytids	Right	Right sided vision loss (NLP) Pain and fullness behind right eye Right RAPD Limited EOM Exotropia and Hypotropia Ecchymosis and induration above medial brow Subacute infarctions in frontal, parietal, and occipital lobes	Approximately 24 h	Ocular massage Topical timolol 0.5% Brimonidine 0.2% Oral steroids Intravenous antibiotics	Vision remained at NLP at 1 year Improvement in EOM starting week 2 Scarring and hard nodules in the right glabellar region at 1 year
Kim *et al.* (2013)[9]	30-year-old male	Calcium hydroxyapatite	Nose	Bilateral	Vision loss bilaterally (NLP) Blepharoptosis Total ophthalmoplegia Central skin necrosis Reticular pattern affecting nose and frontal area Conjunctival injection and emboli along conjunctival vessels	Unknown	Unknown	Unknown
Roberts *et al.* (2011)[45]	43-year-old male	Poly-(L)-Lactic acid	Periorbital region	Left	Left sided vision loss (LP) Orbital pain Ptosis Fixed and dilated pupil Decreased IOP Enophthalmos Ophthalmoplegia Conjunctival chemosis, paracentral epithelial defect of the cornea with corneal edema, 2-3+ cellular reaction and pigment	Unknown	Unknown	By self-report, vision remained depressed By self-report, improvement in ocular movements and ptosis

NLP: No light perception; EOM: extraocular motility; RAPD: relative afferent pupillary defect; IU: international units; CF: count fingers; LP: light perception; ATA: atmospheres absolute; IOP: intraocular pressure; IV: intravenous.

In cases of temporal hollowing, the frontal branch of the superficial temporal artery and the middle temporal vein should be avoided [Figure 1][12]. The vein lies within the temporal fat pad, while the artery lies within the temporoparietal fascia and travels superficially to above the lateral eyebrow[12,18]. The superficial temporal artery also anastomoses with the supraorbital, supratrochlear and zygomaticotemporal arteries, providing a pathway into the central retinal artery[13]. The author prefers injecting using high G' fillers deep on top of the bone in this high-risk area; however, the exit of the zygomaticotemporal artery traverses into the orbit just above the zygomatic arch, usually more anteriorly, and may also be a source of orbital ischemia. Poly-L-lactic acid is another alternative due

Mehta *et al. Plast Aesthet Res* 2022;9:57 | https://dx.doi.org/10.20517/2347-9264.2022.19

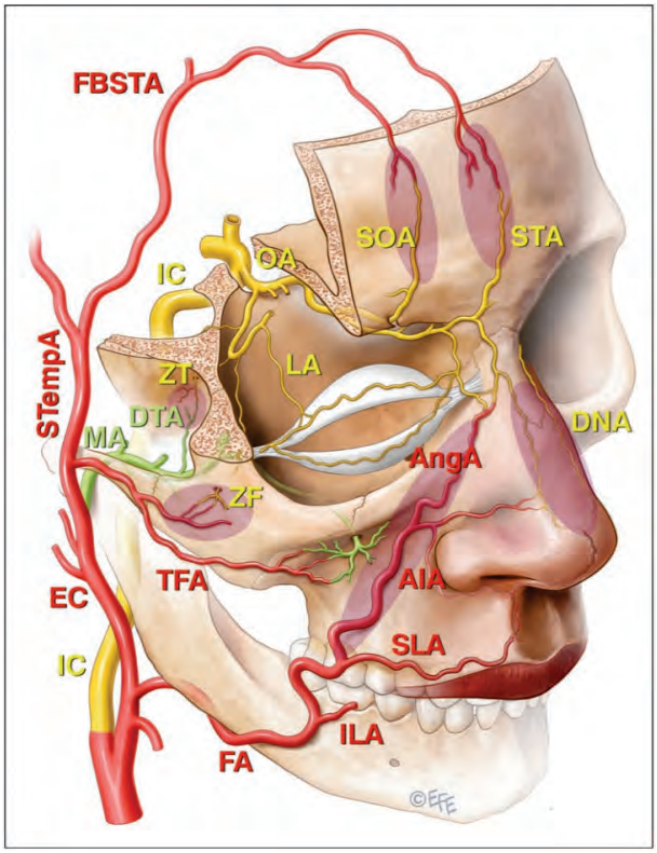


Figure 1. Representative figure of the arteries of the face, ocular, and nasal area. Shaded areas represent communication between the external carotid system and the end branches of the ophthalmic artery (OA) that are implicated in filler induced blindness. This includes the angular branch (AngA) of the facial artery (FA), the transverse facial artery (TFA) that arises from the superficial temporal artery (STempA) and the deep temporal branch (DTA) of the maxillary artery (MA) in the shaded zones. The frontal branches of the superficial temporal artery (FBSTA) anastomoses with the supraorbital (SOA) and supratrochlear arteries (STA), but the FBSTA has not been directly implicated in blindness after filler injections. Other vessels mentioned are the internal carotid artery (IC), external carotid artery (EC), inferior labial artery (ILA), superior labial artery (SLA), inferior alar artery (AIA), dorsal nasal artery (DNA), zygomaticofacial artery (ZF), zygomaticotemporal artery (ZT), and lacrimal artery (LA). Figure and caption reproduced with permission from Goodman *et al.* 2020 by permission of Oxford University Press on behalf of The Aesthetic Society[14].

to the volume available when diluted 8:1 or 9:1 with sterile water and lidocaine. The less viscous preparation is easier to see reflux, if in an artery.

When injecting the cheek, one should be aware of the infraorbital bundle, which lies approximately 1 centimeter below the orbital rim at the medial limbus[19], the transverse facial artery along the zygoma, and the zygomaticofacial artery higher up on the zygomatic arch laterally [Figure 1]. Two main danger zones exist in the infraorbital and cheek area[20]. Periosteal injections for tear-trough deformities or infraorbital hollow correction can be dangerous due to anastomoses of the nasal branch of the infraorbital artery with the supratrochlear artery, dorsal nasal artery, or angular artery[20]. Secondly, for cheekbone enhancement fillers, superficial injections may cause problems with the cutaneous perforations of the zygomaticomalar branch of the infraorbital artery[20]. In these areas, a high G' product is recommended[12]. Additionally, for tear trough deformities, retromuscular, pre-orbital microfat injections may be considered, while for cheekbone enhancement, injections should be performed in supraperiosteal layers. However, fat injections are not reversible, and there is a wide variation in how HA fillers can be reversed[21-23]. For example,

Restylane-Lyft for the cheek takes very little hyaluronidase to dissolve, while Voluma and RHA4 are very difficult to reverse[21-23]. Calcium hydroxylapatite is also not reversible, although some have seen improvement with simple saline diffusion[24], hyaluronidase[25], sodium thiosulfate[26], steroids[27], and 5-fluorouracil injections[28].

Given the vascularity of the nose, filler injections in the nasal area are commonly associated with complications[12,29,30]. Although the major nasal arteries at risk for complications are the lateral nasal artery and dorsal nasal artery, the presence of several anastomoses in the nose also predisposes to blood flow that can be reversed with filler injection[11]. The vasculature typically lies in the subdermal plane above the superficial musculoaponeurotic system [Figure 1][11,12]. The tip and ala of the nose are most commonly prone to necrosis secondary to compression or vascular injury[12]. If one were willing to risk injecting this area, one author recommends reassessing the patient 15 min after injection to check for vascular compromise[12].

The superior labial artery (SLA) and inferior labial artery (ILA) also have variability in their course and depth[31]. While the SLA is not very likely to be found subcutaneously at the vermillion border, the vasculature is superficial in the midline and Cupid's area, which can carry a high risk[31]. Additionally, the lips become thinner with aging, which may predispose the arteries to intravascular injection[31]. Therefore, for lip injections, injections should be limited to approximately 3 mm depth in order to avoid the SLA and ILA that course deeper within the lip[12].

In cases of jawline contouring, one study found an anatomic variation in which the transverse facial artery travels from the masseter muscle to the angular artery and dorsal nasal artery[32]. This could be one pathway for how lateral face injections, including masseter and jawline contouring, could lead to blindness[32]. Toure *et al.* recommend a safe zone for injection below a line from the lobule of the auricle to the labial commissure[32]. The facial artery branches into the submental artery and ascending submental artery, which, if cannulated, can lead to skin necrosis of the lower face[33].

COMPLICATIONS

Vision loss

As cited in the introduction and the Table, there are at least 211 cases of blindness reported in the English literature as of January 2022, and the actual number is likely many folds higher, since most cases are not published in literature. The presentation of a patient with vascular occlusion of the ophthalmic artery involves blindness and periocular symptoms, usually very soon after filler injection, and can present with concurrent ptosis and ophthalmoplegia[29,34]. In a recent review paper, 35 out of 39 cases had immediate vision loss symptoms and 2 cases developed symptoms within 10 min[29]. However, in several cases, the symptoms developed a day after injection[29]. The etiology of this vision loss is usually due to retrograde arterial embolism into branches of the ophthalmic artery, including the retinal branches[35-37]. The glabella, temple, and nasolabial folds have vasculature that commonly anastomoses to the ophthalmic artery[38]. Thus, the most common locations that cause vision changes are the nasal region, followed by the glabella, forehead, and nasolabial folds[5,39]. The most common occluded vessels are the ophthalmic artery, central retinal artery, branch retinal artery, and naso ciliary artery[29,30]. Occlusion of the ophthalmic artery is usually secondary to injections in the nose, while occlusion of the retinal artery is secondary to glabellar injections[30]. Given the various anastomoses in the different facial arteries, there are several injection locations that can cause ocular complications.

A recent study found that filler particles disintegrate into smaller particles immediately after injection, supporting the hypothesis that emboli, rather than a column of filler, cause an obstruction[40]. Another study

further supported this idea by showing that the force required to push a column of filler retrograde was higher than the normal injection force[41]. However, one study also found that only 0.085 mL was required to fill the supratrochlear artery from the glabella to the ophthalmic and central retinal artery bifurcation, highlighting that even a small volume of filler could cause this complication[42]. Per the 48 published case reports by Beleznay *et al.* of filler-induced vision changes, 81% of cases were treated with hyaluronic acid filler followed by calcium hydroxylapatite (10.4%), and one case each was from autologous fat and poly-L-lactic acid (PLLA)[5]. This is likely secondary to the fact that hyaluronic acid is the most common type of filler injected, followed by autologous fat and calcium hydroxylapatite[39]. However, visual loss has even been noted to occur secondary to platelet-rich plasma (PRP) injections and PLLA injections[43,44]. In the 4 reported cases, one woman developed painful vision loss with no light perception in the left eye after PRP injection into the left glabellar region[43]. Her fundus exam was suggestive of an embolus within the central retinal artery[43]. At her 1-month visit, she was noted to have a pale optic disc with pigment in the superior temporal region and developed a retinal detachment 8 months after her initial injection[43]. In one reported case of blindness secondary to PLLA, a patient received an injection in the left periorbital region and reported immediate pain in the left eye as well as blurring of vision[44]. On exam, the patient was found to have a decrease in vision to light perception with projection, a fixed and dilated left pupil, as well as ophthalmoplegia and ptosis[44]. While the ophthalmoplegia and ptosis improved over time, the patient's vision still declined[44].

Although irreversible damage to the retina has been previously studied to occur within 90 min, a recent study found that retinal infarction can happen as early as 12-15 min after complete occlusion[45,46]. Given the low incidence of cases, no high-level studies currently exist that allow for a clear management recommendation for this devastating complication[47]. Ocular physical maneuvers, including compression and paracentesis, are a rapid intervention[47,48]. An ocular massage can be performed with manual firm compression to the globe in 10-20 second intervals followed by a sudden release. This compression can be performed with a Goldman lens or trans palpebral with 2 fingers[47]. The goal of these maneuvers is to lower the intraocular pressure, dilate the occluded artery and allow for the migration of the emboli to a peripheral vessel, preserving central vision[47]. Rebreathing in a brown paper bag for 10 min every 30 min can also increase CO_2 and cause vasodilatation[49]. Methylprednisolone and other intravenous steroids can be used to decrease the retinal edema caused by damage to the cells[11,47]. Intraocular pressure reduction can be achieved with timolol, mannitol, and acetazolamide to restore retinal vascular flow and avoid visual loss[47]. Lastly, hyperbaric oxygen (HBOT) can be used when available, as it provides a subjective relief and can also work to improve plasma oxygen concentration and dilate the retinal arteries[47,50]. While nitroglycerin paste has been considered, questions remain on whether it is able to penetrate the deep orbital vessels[47]. One study with a rabbit eye model found that there was no improvement in perfusion with nitroglycerin paste, and the veins were also found to have a more congested appearance[51]. Additionally, dilation of the arterioles could push the product further into the smaller arterioles and capillaries[51]. The use of hyaluronidase can also be considered, especially when the filler is HA-based, within 60-90 min after visual loss[47]. While hyaluronidase has been noted to also be administered outside the 90-min window, the newest cases have not been able to show significant improvement in visual acuity.

There has been some interest in the use of HBOT in the treatment of ophthalmic artery occlusion. HBOT is defined as an intervention in which an individual "breathes near 100% oxygen intermittently while inside a treatment chamber at a pressure higher than at sea level pressure (> 1 atm)[52]." The main goal is to increase the amount of oxygen dissolved in the plasma. Increased dissolved oxygen works to improve the diffusion distance, supporting oxygen-dependent processes that do not get enough arterial blood supply[53]. One report discussed the case of a 31-year-old woman who received HA filler at the nasal dorsum and developed

immediate vision loss in the right eye[54]. After being diagnosed with central retinal artery occlusion, she received a multitude of treatments including high-flow O_2, ocular massage, steroids, and blood thinners[54]. She also received daily 90-min therapy of HBOT at 2.5 atmospheres absolute (ATA) or 253 kilopascals (kPa) for 3 weeks. However, the patient had no improvement in the vision in the right eye, with her visual acuity remaining at no light perception[54]. In another case, a 49-year-old woman was also found to develop a central visual defect in her right eye after the injection of poly-L-lactic acid (PLLA)[55]. Her visual acuity was found to be 20/200 in the right eye. She received ocular massage, brimonidine, and HBOT (unknown pressure) twice daily for 5 days, but did not have any improvement in her vision[55]. A 41-year-old woman who had vision loss in her right eye after a forehead filler injection received retrobulbar hyaluronidase and 2 h of daily hyperbaric oxygen therapy, among other treatments[56]. This patient had recovery of vision from no light perception to hand motion[56]. It appears that an optimal HBOT protocol is daily use for several days or weeks after the onset of blindness. The typical HBOT protocol for compromised grafts and flaps is 2.0 to 2.5 ATA for 90 to 120 min twice a day, and it appears that preliminary case reports are following that protocol[52]. While the use of HBOT has been shown to have some effect on skin vascular occlusion, discussed later in this review, there is still the question of whether HBOT has the same effect on visual loss from occlusion. It is worth noting that data from studies solely looking at artery occlusions outside of emboli from facial filler have documented some improvement with HBOT[57-60]. The disease processes in these studies looked at idiopathic CRAO and Factor V Leiden mutations[57-60]. However, at this stage, the data for HBOT for ophthalmic artery occlusions and central retinal artery occlusions secondary to facial filler emboli remain preliminary and inconclusive.

The use of hyaluronidase through a retrobulbar injection is currently being debated and further studied. A 2018 case report discussed a retrobulbar injection of 450 IU of hyaluronidase, which completely restored a patient's vision after receiving HA filler injections near the infraorbital neurovascular bundle[61]. However, this report did not document an objective visual acuity before and after hyaluronidase treatment. Another case study also showed improvement from light perception to hand motion and eventually full recovery after 2 injections of 900 IU retrobulbar hyaluronidase, 4 and 5 days after filler injection[62]. Given that these cases are anecdotal and not controlled studies, it is unclear if an improvement in vision would have occurred without retrobulbar hyaluronidase. Additionally, other reports have not shown improvement or been as definitive as to whether this treatment is a viable solution[63,64]. An animal model study showed that extravascular injection of hyaluronidase was not able to penetrate the vascular lumen or re-perfuse occluded auricular arteries[65]. This is supported by Hwang *et al.*, in which 1000 IU of retrobulbar hyaluronidase within the ophthalmic artery 30 min after occlusion in rabbits was unable to relieve the obstruction[66]. However, in contrast, Lee *et al.* injected hyaluronic acid into the ophthalmic artery, confirmed ischemia with fundus photography, and then injected retrobulbar hyaluronidase[67]. While initial experiments with 1500 IU did not show any improvement, 3000 IU of hyaluronidase 5-10 min after occlusion showed an improvement in perfusion, possibly secondary to higher dosing and faster treatment[67]. Questions were raised about the methodology in the Lee *et al.* study regarding the lack of documented electroretinogram testing prior to treatment with hyaluronidase to detect a complete occlusion[67,68]. Hwang *et al.* found that the fundus photographs seemed to support a branch retinal artery occlusion rather than a complete retinal artery occlusion, possibly indicating only partial vision loss prior to treatment[68]. Additionally, the authors discuss that a dose of 3000 IU could lead to a compartment syndrome with readily available preparations (since the powdered form is not widely used in the US) and injecting within 5-10 min of occlusion would prove to be very difficult in the clinical setting[68]. Another *in-vitro* study showed that hyaluronidase could not cross the dural sheath of the optic nerve, which can prevent access to the central retinal artery[69]. Ugradar *et al.* also found that hyaluronidase was not able to reduce the particle size in a substantial manner, creating particles that were still greater than the size of the vessel[70]. These *in-vitro* studies highlight that physiologically, it is difficult to replicate how retrobulbar hyaluronidase can effectively relieve filler

obstructions. This translates to what has been seen clinically as well, in that some patients have a full recovery of vision with retrobulbar hyaluronidase while other cases do not[29]. An additional literature review concluded that the efficacy of retrobulbar hyaluronidase was not clear and that there was not enough evidence to support retrobulbar hyaluronidase given the inherent risks[48]. This treatment has a level of evidence V, which confers a grade D recommendation from the American Society of Plastic Surgeons[48,71].

A more novel way to treat blindness from filler complications may be to consider it a stroke, because the optic nerve is part of the central nervous system. Activating a stroke protocol may be prudent. Baley-Spindel *et al.* noted the occlusion is likely composed of both HA gel and red thrombi; therefore, a combination of hyaluronidase and alteplase yielded the best results in clearing HA gel thrombi in their rat model[72].

Ophthalmoplegia/Double vision

While vision-threatening complications are better known, facial fillers have also been seen to cause ophthalmoplegia, as noted in Table 1. A recent study showed that 50% of patients with occlusion of the ophthalmic arfpresentation is not always as cleartery also presented with ophthalmoplegia[73]. Another study found that 15 (71%) of 21 patients over a 9-year period with artery occlusion also developed ophthalmoplegia at initial presentation, with an average of 2.8 rectus muscles involved[74]. The mechanism behind this is theorized to be from ischemia to the cranial nerves or extraocular muscles[74,75]. However, a recent report of 2 isolated ophthalmoplegia cases illustrated that this side effect could also be secondary to an inflammatory response[76].

Management of ophthalmoplegia, if a hyaluronic acid (HA) filler is used, can be performed with 1500 IU of hyaluronidase subcutaneously around the site of injection, and in the case reported by Bae *et al.*, hospitalization was required[77]. Even though the ophthalmoplegia is resolved in some cases, sometimes the ocular misalignment persists, requiring strabismus surgery[76]. In the 2 case reports where an ischemic etiology was not suspected, one patient improved after Medrol Dosepak and aspirin 81 mg, and the other did not improve as she presented 3-4 months after the complication[76].

Soft tissue necrosis

The presentation of a patient with vascular occlusion is often characterized by pain disproportionate to the injection, along with blanching[78]. This is followed by livedo reticularis secondary to venule swelling[79,80]. However, in a clinical setting, the presentation is not always as clear, with pain often not accompanying these events[81]. For example, a net-like reddish/blue appearance may be hard to distinguish from bruising or simple erythema, but a delayed capillary refill would support ischemia. A recent study also showed that in a survey of 52 injectors, 62% had reported one or more intravascular injections, highlighting the frequency of these events[81].

The etiology of vascular complications involves arterial compromise causing tissue anoxia and progression to necrosis[15]. As the filler is being injected, it may flow in either direction in the vessel, and lead to an obstruction of the blood supply[15]. Given that fillers have inherently different properties in viscoelasticity and cohesivity, the outcomes have different severity[3,15]. Case reports with polymethylmethacrylate (PMMA) have had complications showing more dramatic skin necrosis compared to other fillers[82-84].

The glabella, nose, and nasolabial folds are at higher risk because they depend on a single arterial branch[13]. Out of all the cases of vascular necrosis, nasolabial fold injection was associated with the highest number of cases, followed by injections into the nose[85]. Nasal necrosis is likely secondary to the dorsal nasal artery having variable anatomy, occurring only 34% of the time as a pair of arteries, with other variations including

a single large dorsal nasal artery or in random distribution[86]. Given the potential for embolization of facial fillers, vascular complications also have been seen to occur far from the injection area in the mid and lower face. The vascular supply of the internal nose arises from branches of the superior labial artery, the sphenopalatine artery, the posterior ethmoidal artery and the anterior ethmoidal artery[87]. After an injection of HA above the anterior nasal spine and nasal bones, a 42-year-old female developed gingival necrosis of the right upper incisor, partial lip mucosa necrosis, and an exophytic palatal lesion[87]. The gingival necrosis was likely related to embolization of the septal branches of the superior labial artery and compression of the distal arteries from the septal branch of the posterior ethmoidal artery[87]. In one author's personal experience, she received an injection of hydroxylapatite in her left cheek, in which she noted that the needle was directed somewhat tangentially. After injection, she immediately developed blanching and mottling, which later took on a reticulated appearance due to the involvement of the infraorbital artery. She did not receive hyaluronidase at that time. The following morning, the mottling of her skin extended towards her lower eyelids and the left nasal bridge [Figure 2]. On day three, she developed pustules, necrosis of the skin, and eventually left permanent scarring [Figure 3]. Her erythema of the gums was suggestive of infraorbital artery involvement [Figure 4]. Injections into the infraorbital artery may be performed from the cheek augmentation, with the subsequent embolization extending to the facial artery below.

Skin necrosis has also been seen to occur from filler injected into the lower face. One patient, after receiving dermal fillers in the lip to correct an atrophic scar, presented with pain and blanching of the upper lip with a blue tinge 2 hours after her initial injection[88]. The authors did note that the necrosis may have been secondary to an alteration of the blood vessel course from scarring already present in the area[88]. Injections in the lower lip may need to be cautious of the inferior labial artery, which has been studied to have variation in its dominant arterial sources [Figure 5][89].

Skin necrosis with chin injections has also been reported[90,91]. In one case, the patient developed numbness on the right side of her tongue during an injection of her chin and was found to have an obstruction of her deep lingual artery[90]. In another case, after chin augmentation injection, a patient developed pain with swallowing as well as livedo reticularis and mottling from the mental crease to the upper cervical area 10 min after injection[91]. Pain with swallowing can be explained by ischemia in the submental branches supplying the digastric, mylohyoid, and platysma muscles[91]. It is worth noting that the main blood supply of the chin comes from the ascending mental artery, branching off the submental artery[33]. If that ascending mental artery is cannulated, the filler can travel retrograde to the submental artery and facial artery, causing infarction to the lips, nasolabial fold, nose, and paranasal skin[33]. Additionally, if filler travels through the submental artery and crosses anastomosis to the sublingual artery, it can also cause necrosis of the root of the tongue and floor of the mouth through the involvement of the dorsal lingual and sublingual arteries[33].

If vascular occlusion is suspected with pallor and blanching, the injection must be stopped immediately[13,78,92]. Aspiration of the product should be attempted before withdrawing the needle[13,78]. With the goal of improving blood flow, warm compresses and a massage of the area should be done[13,76,90]. Regardless of filler type, hyaluronidase should be injected as it has been shown to reduce edema[93,94]. Aspirin should also be started to limit clot propagation and platelet activation and be given with an antacid[13,92]. In one case report, low level light therapy (LLLT) was used with the intention of reducing pain and inflammation, and improving tissue repair and regeneration[77]. The goal of LLLT is to use photons at a non-thermal value to change biological activity[95]. Through the enhancement of specific enzyme activity, LLLT has been shown to activate intracellular signaling pathways and transcription factors involved with cell proliferation, survival, and tissue repair[95]. Nishioka *et al*. have also shown that LLLT therapy increases skin flap viability in rats, with the percentage of necrosis area of the flap decreasing in the LLLT group[96].

Mehta *et al. Plast Aesthet Res* 2022;9:57 | https://dx.doi.org/10.20517/2347-9264.2022.19

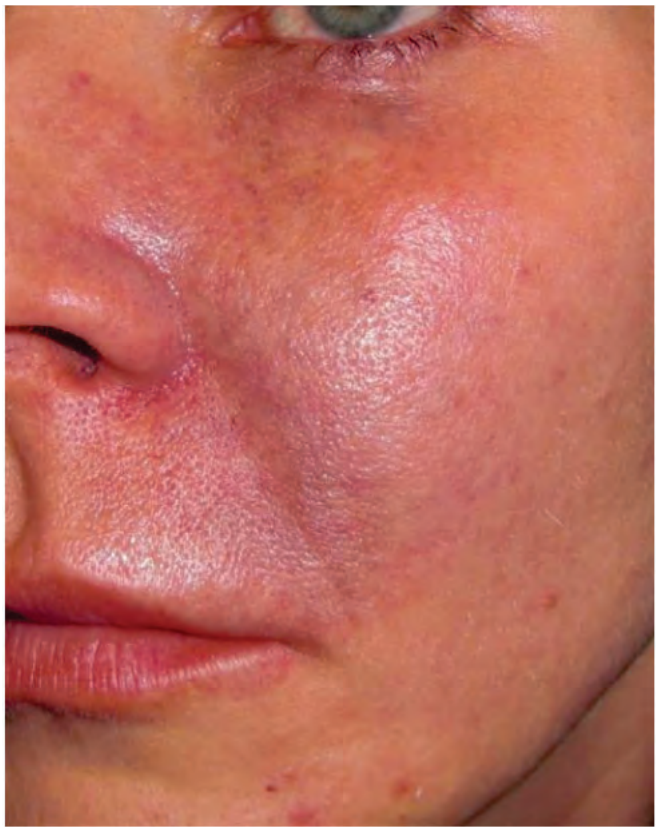


Figure 2. Mottling of the skin the morning after cheek injection, extending from the lower eyelid to the upper lip and part of the nose due to involvement of the infraorbital artery.

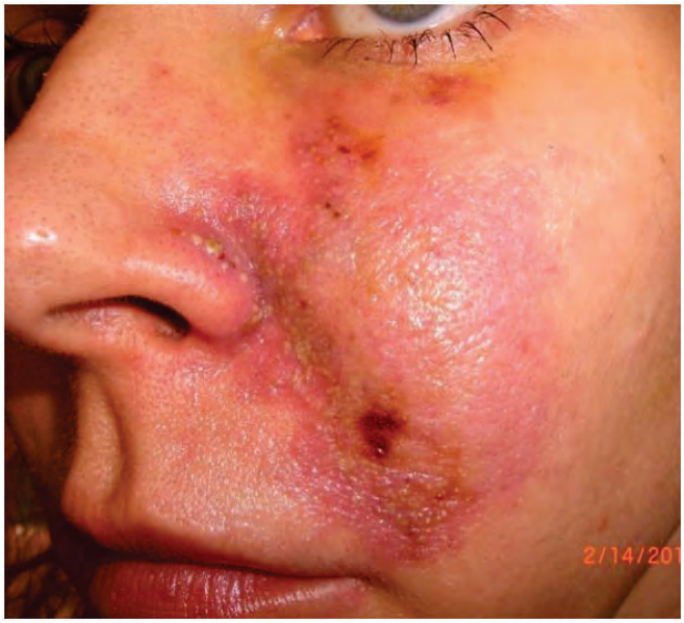


Figure 3. Formation of pustules on the nose and a full thickness defect near the nasolabial fold 3 days after injection due to involvement of the facial artery.

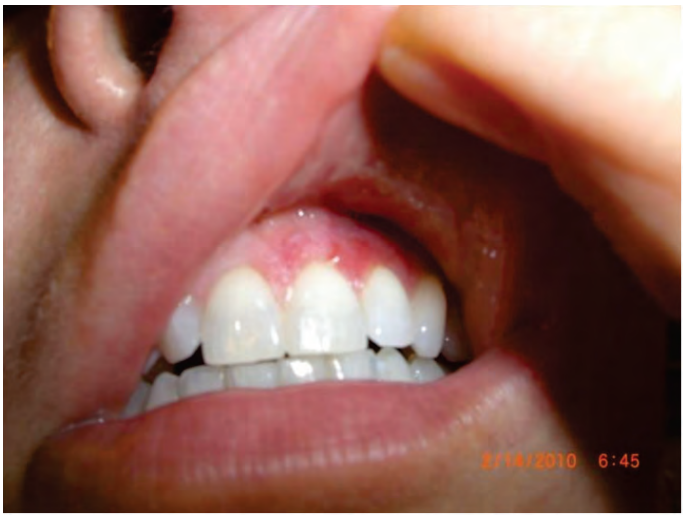


Figure 4. Erythema of the gums indicating involvement of the infraorbital artery.

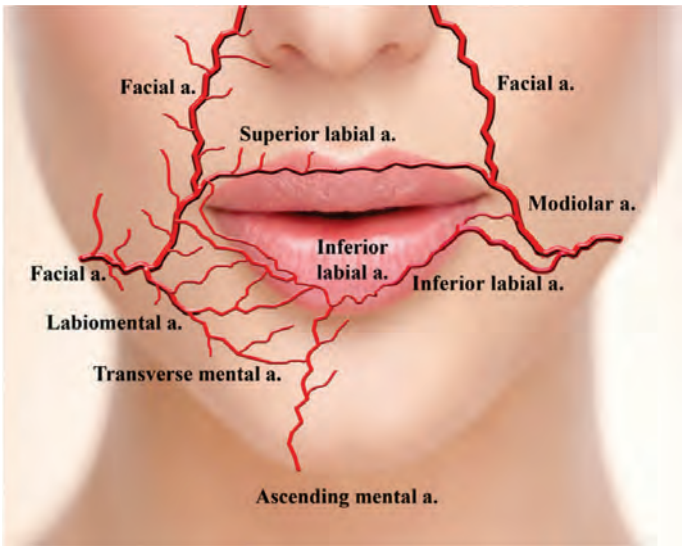


Figure 5. Representative figure of the main arteries of the lower face and chin, with depiction of the variation of arterial sources of the inferior labial arteries. Figure reproduced from Tansatit *et al.*[89].

Sildenafil, tadalafil, and vardenafil can also be used to relax smooth muscles, dilate blood vessels, and increase blood flow[97]. The use of nitroglycerin has not been fully defined. Although nitroglycerin paste has innately vasodilatory properties, an animal study showed no improvement in perfusion and raised the question of whether arterioles dilation could cause further propagation of filler and worsen the ischemia[51]. Given its inherent risks of headaches and hypotension, van Loghem *et al.* did not make a clear recommendation on whether to incorporate nitroglycerin paste[13].

Hyperbaric oxygen has also been reported to be an effective adjunct treatment for vascular occlusion. A 32-year-old female who developed vascular occlusion after HA filler on her nose received 1 month of biweekly 90 min HBOT sessions at 2.4 ATA, after which her nose showed improvement in vascularization[98]. Another report also remarked on a 37-year-old female who developed ischemic changes to her face after an

injection on her proximal temple[99]. After receiving 6 treatments twice daily (2 treatments at 3.0 ATA followed by 4 treatments at 2.4 ATA), the patient showed improvement in ischemic discoloration[99]. Two cases, one involving a 46-year-old man who received poly-methylmethacrylate and calcium hydroxylapatite and a 40-year-old white woman who was treated with hyaluronic acid, showed improvement in their skin necrosis after HBOT[94]. One treatment lasted 14 days, while the other lasted 2 days[94]. Thus, while HBOT remains an inconclusive treatment for vascular occlusion of the ophthalmic and retinal artery, it has been shown to potentially have more benefit in skin necrosis treatment.

Recently, a new protocol has been released in which high dose pulsed hyaluronidase is used for vascular adverse events. For low volume events (0.1 mL or less of HA filler), 450 IU of hyaluronidase is used in a single area, for an area half of an upper lip[100]. If the nose has involvement, 900 IU of hyaluronidase should be used[100]. The dosing should also be hourly rather than the traditional daily dosing to maintain high concentrations in the ischemic zone[100]. The injections should be given at injection sites, and if there are distal sites that appear ischemic, one should consider injecting distal sites of ischemia[15]. Delorenzi *et al.* have remarked that hyaluronidase is able to diffuse through an arterial wall, so the most important area of injection would be areas that show ischemia[15]. However, the article did comment on a case in which the patient did not initially improve with hyaluronidase injection into the ischemic tissue, but showed improvement after hyaluronidase was injected into the affected artery[15]. Thus, further studies may be needed to elucidate the most effective area for hyaluronidase injection immediately after vascular occlusion.

Cerebral infarction

Filler injections can lead to very severe complications. Cerebral infarction secondary to vascular occlusion has been noted as a complication of filler injections. A review article of 44 cases showed that 8 patients (18.2%) had CNS involvement, including upper limb weakness, acute infarction, or hemorrhage[29]. A 20-year-old female who presented with non-improving vision loss in her right eye was found to have multifocal infarcts in her parietal lobes[101]. This patient received injections in the glabella, an area known to cause combined ophthalmic and cerebral complications[101]. Anatomically, the supratrochlear and supraorbital arteries were injected with enough force that the filler traveled retrogradely to enter the cerebral circulation via the Circle of Willis[101]. Another study involved a 39-year-old female who presented with vision loss in the left eye after filler injection into the glabella[102]. This vision loss was concurrent with ptosis and total ophthalmoplegia[102]. The next day, an MRI found several cerebral infarctions that were embolic in nature[102]. After one week, the infarction transformed into a parenchymal hematoma, after which the patient received methylprednisolone[102]. While her limb weakness improved, she continued to have a right arm monoparesis[102]. Another case involved a 40-year-old female who developed a cerebral infarction after nasal augmentation[103]. With a GCS of 4 and on mechanical ventilation, the patient developed gastric ulceration, pulmonary infection, respiratory failure, and cerebral herniation, dying 6 days after the filler injection[103]. For this patient, the theory was that there were several small HA particles in the capillaries from this filler injection[103]. The authors recommended immediate thrombolysis within the 12-h window of functional impairment (90 min for concomitant ophthalmic arterial occlusion) and consideration of decompressive craniectomy[103].

PREVENTION

Given the severity of these intravascular complications, prevention is key in delivering high-quality patient care. Knowledge of various injection techniques and the relatively new utilization of imaging have been studied in the prevention of these outcomes.

Injection techniques

There are several injection techniques that have been studied to help prevent vascular occlusions. Aspiration before injection (with an unprimed needle, especially if the filler is thick or sticky) and using lower volumes of the product (0.1 mL) can help indicate that the needle has not entered a blood vessel and reduce the severity of complications if a blood vessel is entered[7,17]. Sometimes aspiration can give you a false sense of security, as the filler may be too thick to detect reflux of blood when in a vessel. If injecting in the areas of the supratrochlear artery, supraorbital artery, and dorsal nasal artery, compression of the vessel pathway can help prevent retrograde flow[104]. The use of a reversible HA filler will allow for treatment with hyaluronidase if a reversal of vascular occlusion is needed[7]. Given that the pressure of the filler injection can cause retrograde flow, injecting at a slow pace can help in preventing complications[7,105].

Needle size has also been seen to have an impact on vascular obstruction. While a smaller needle may improve the precision of the injection, it may increase the likelihood of penetrating the vessel wall rather than a larger bore needle which would roll on the side of the artery[15,104]. Additionally, more pressure is required to inject through a smaller bore needle which could lead to more pressure into a vessel, should vasculature be entered. A recent study also found that the use of microcannulas had 77% lower odds of occlusion compared to needle injections, due to the fact that blunt tips could avoid piercing vessel walls[106]. However, small bore microcannulas still have the potential to penetrate the facial artery with a small amount of force (0.23 kg for a 27G cannula)[107]. Epinephrine may also help with vasoconstriction, but may make it more difficult to distinguish an early manifestation of necrosis[104]. Thus, administering local anesthesia without epinephrine may be considered[104,108].

Imaging

Mapping vasculature to prevent intravascular filler injection

Various studies have now started incorporating ultrasound as a method to map vasculature and reduce the incidence of vascular complications seen with filler injections. Doppler ultrasound has been seen to detect anatomy, such as the facial artery lateral to the nasolabial fold, along with its different anatomical variations[109]. One other study commented that although ultrasound may be difficult to manage in conjunction with injection, a new technique combining 3D time of flight magnetic resonance angiography (3D-TOF MOTSA MRA) and infrared (IR) facial heating could visualize the following arteries: facial, angular, superior labial, inferior labial, lateral nasal, dorsal nasal, supratrochlear, supraorbital, and superficial temporal[110]. These images could be acquired on a 1.5 or 3 Tesla (T) system with a head coil, with an additional surface coil on top, to improve signal reception[110]. The authors showed that these MRA images could be projected on the patient's face before injection, albeit without the same 3D depth aspect[110]. The main benefit of this method was visualization of the facial arteries in a non-invasive and contrast-free manner[110]. However, the cost of MRI in these individual countries may need to be considered before the widespread adoption of this technology. Our team has also looked at the utilization of 7T MRI and shown its ability to depict small orbital and eyelid structures, as well as the orbital branch of the infraorbital artery (article in press).

The use of ultrasound has been adopted at various points in the filler injection procedure. Firstly, ultrasound has successfully determined that the needle or cannula is positioned in the correct plane and not within or near a vessel[111]. Schelke *et al.* discussed how the use of doppler ultrasound can help distinguish vessels as well as the direction of blood flow [Figure 6][112]. Rocha *et al.* recommended that once the needle or cannula is determined to be in the correct location, the filler can be injected without aspiration[111]. After the injection of filler, doppler ultrasound can again be used to confirm the vascularization of the area[111]. As seen in Figure 7, the placement of filler deposits, such as hyaluronic acid, can be distinctly visualized on ultrasound to confirm correct depth and placement.

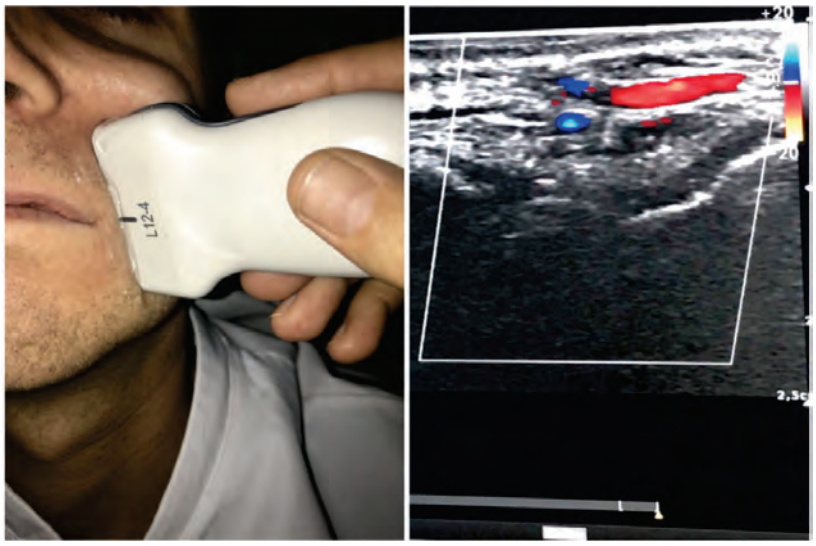


Figure 6. Localization of the artery with ultrasound. Figure reproduced with permission from Schelke *et al.*[112].

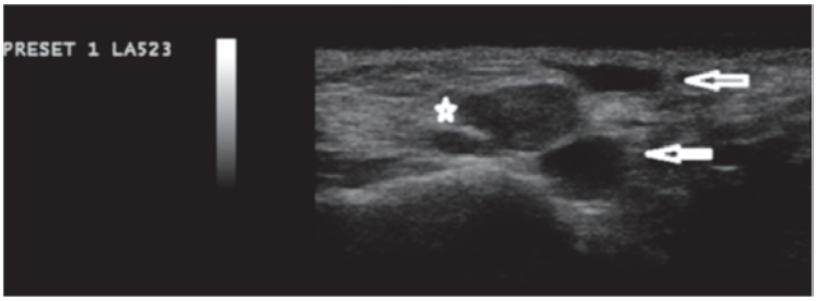


Figure 7. Multiple deposits of hyaluronic acid filler, as represented by the two anechoic deposits and one hypoechoic deposit. Figure reproduced with permission from Schelke *et al.*[112].

Diagnosing areas of ischemia from filler complications

Imaging can also be used in the early diagnosis and treatment of filler complications. Another study evaluating laser doppler imaging (LDI) found that LDI was able to accurately delineate a hypo-perfused area to help target hyaluronidase treatment[113]. Color Doppler flow imaging (CDFI) was able to successfully detect retinal artery occlusions and ophthalmic artery caused by filler injections by showing decreased retrobulbar blood flow[114]. Doppler ultrasound may be able to be used to detect the lack of perfusion, and in rare cases, an ischemic vessel may be able to be injected with hyaluronidase under ultrasound guidance. Schelke *et al.* reported on a case of how, upon crusting under the lip after upper lip augmentation, 150 U of hyaluronidase was injected with ultrasound guidance[112]. A case in which ultrasound was used to inject hyaluronidase into a visualized filler deposit is seen in Figure 8. In another case, after a patient presented with mottling of her chin following filler injection, ultrasound was used as guidance for hyaluronidase injection [Figure 9]. Ultrasound imaging appears to be valuable in helping the injector decide where to place the hyaluronidase. However, this may be very difficult to do, and it is unclear how much an ultrasound may help or distract from the process of trying to cannulate a vessel.

Magnetic resonance imaging (MRI) has also been studied as the primary mechanism to evaluate for infarctions after ischemic complications. Many of the case reports that were reviewed showed that an MRI

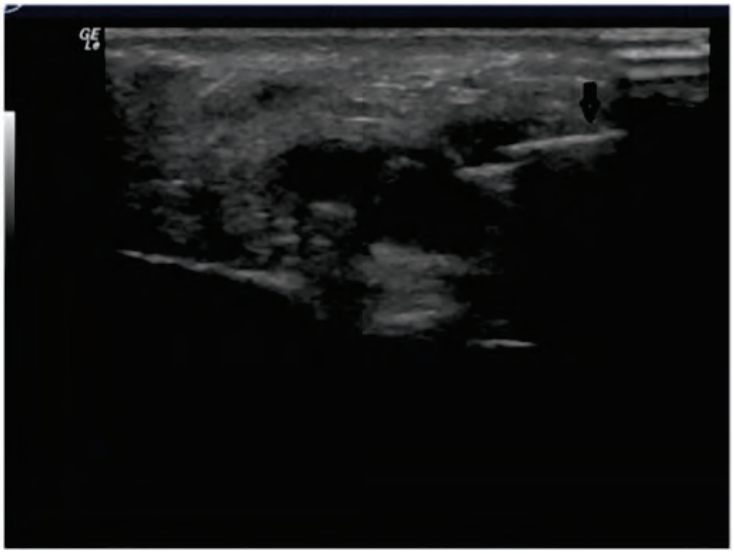


Figure 8. Needle inserted into filler deposit under ultrasound guidance. Figure reproduced with permission from Schelke *et al.*[112].

or magnetic resonance angiography (MRA) was used to evaluate intracranial infarctions and embolisms[101,102,115]. Additionally, the use of MRI is finding an increasing role in the detection of other non-ischemic complications associated with fillers such as inflammation, foreign body granulomas, and filler migrations, which we will expand upon in another review paper[116]. While the use of imaging in this field is still relatively recent, it represents an area for further development and utilization.

REVERSIBILITY

Understanding the reversibility of fillers is important, should an ischemic or non-ischemic complication occur. Fat and calcium hydroxylapatite are not reversible, although some reports have seen improvement in calcium hydroxylapatite injections with simple saline diffusion[24], hyaluronidase[25], sodium thiosulfate[26], steroids[27], and 5-fluorouracil[28] injections. Additionally, many of the new hyaluronic acid gel fillers require high doses of hyaluronidase and multiple injections to reverse. For example, Restylane-L and Restylane-Lyft are easy to dissolve, whereas the Vycross products, RHA3-4, and the newer Restylanes are much more difficult to reverse. Refer to previous publications[21-23] and upcoming papers to remain updated on all the different filler products.

CONCLUSION

As filler injections become more widespread, it is important to be aware of and know how to manage the devastating ischemic complications that can occur. Most of these ischemic complications occur with pain disproportionate to the injection and with a sudden change in vision or blanching or dusking of the skin. Ischemic complications may also present in a more delayed fashion in the first day or two after injection with mottled reticular-appearing skin. Treatment of ischemic complications begins with early identification of the ischemia, including being aware of cerebrovascular events, and early treatment of ophthalmic artery occlusions within 90 min. Aspirin and other anticoagulation can be used, but the main tool is early delivery of hyaluronidase of 450-3000 units in areas that can accommodate that volume, spread over multiple boluses, depending on the area and severity of ischemia. Cannulating an artery, perhaps with image and doppler guidance, for hyaluronidase injection would be ideal, but this is very challenging. For blindness, activating a stroke protocol at a nearby hospital may even be considered to treat the red thrombi component of arterial occlusions. Warm compresses and ocular massage (for ocular ischemia), hyperbaric oxygen

Mehta *et al. Plast Aesthet Res* 2022;9:57 | https://dx.doi.org/10.20517/2347-9264.2022.19

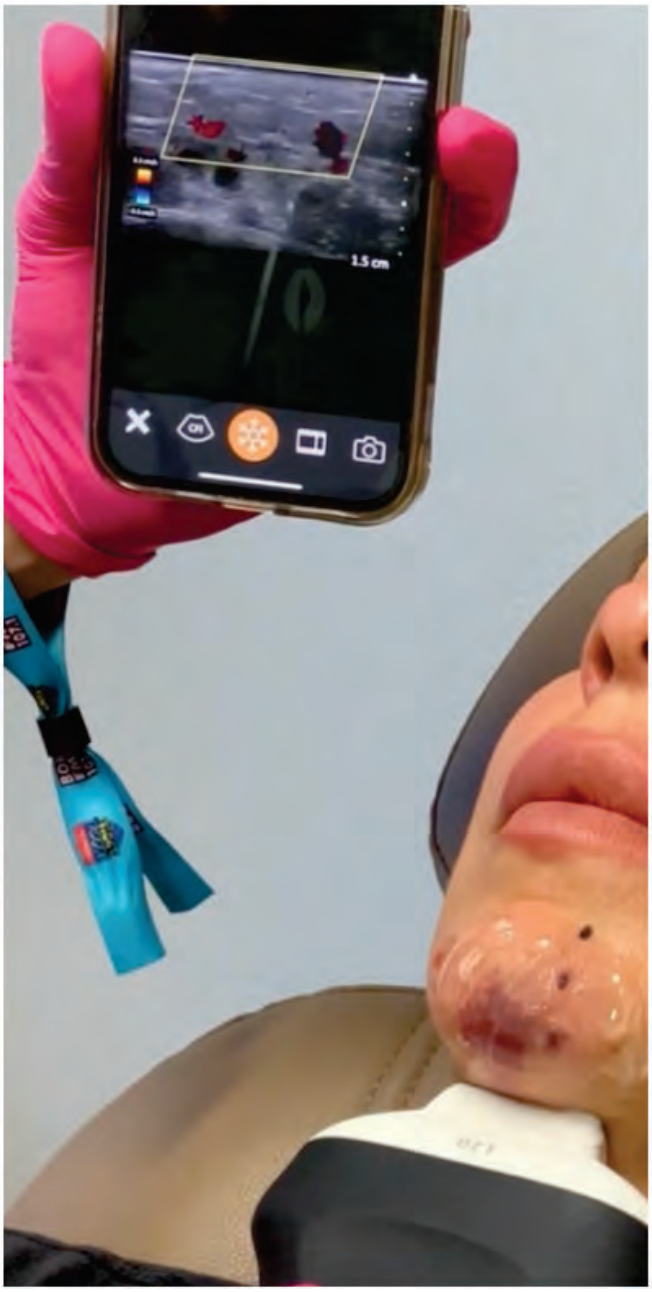


Figure 9. Using ultrasound (Clarius Portable Ultrasound L20) in a clinical setting to localize filler placement causing skin ischemia and injecting hyaluronidase (see Supplementary Video 1 and Supplementary Video 2)

therapy or low-level light therapy (for soft tissue ischemia) can also be considered. Nitroglycerin paste is controversial. Hyperbaric oxygen can be considered to help salvage marginal tissue that may otherwise become necrotic. No panacea exists except for prevention. Due to simple mathematics, occlusion may not be entirely avoidable if one is injected enough, despite one's best efforts. However, minimizing the incidence of these complications requires knowledge of the local anatomy, filler properties (reversible non-permanent filler is safer), and utilizing the safest injection techniques. New advances in the field include utilizing imaging to help avoid and diagnose intravascular injection. Higher concentrations of hyaluronidase may

also be required to reverse the thicker and newer hyaluronic acid gel fillers.

DECLARATIONS

Authors' contributions

Made substantial contributions to conception and design of the study and performed data analysis and interpretation: Mehta P, Kaplan JB, Zhang-Nunes S

Availability of data and materials

Not applicable.

Financial support and sponsorship

This work was supported by an unrestricted Grant to the Department of Ophthalmology from Research to Prevent Blindness, New York, NY and the Keck School of Medicine Dean's Research Scholar Award.

Conflicts of interest

All authors declared that there are no related conflicts of interest.

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

REFERENCES

1. ISAPS International Survey on Aesthetic/Cosmetic Procedures. Available from: https://www.isaps.org/wp-content/uploads/2020/12/Global-Survey-2019.pdf [Last accessed on 1 Sep 2022].
2. FDA Executive Summary General Issues Panel Meeting on Dermal Fillers. Prepared for the meeting of the general and plastic surgery devices advisory panel. Available from: https://www.fda.gov/media/146870/download [Last accessed on 1 Sep 2022].
3. Heitmiller K, Ring C, Saedi N. Rheologic properties of soft tissue fillers and implications for clinical use. *J Cosmet Dermatol* 2021;20:28-34. DOI PubMed
4. Murthy R, Roos JCP, Goldberg RA. Periocular hyaluronic acid fillers: applications, implications, complications. *Curr Opin Ophthalmol* 2019;30:395-400. DOI PubMed
5. Beleznay K, Carruthers JDA, Humphrey S, Carruthers A, Jones D. Update on avoiding and treating blindness from fillers: a recent review of the world literature. *Aesthet Surg J* 2019;39:662-74. DOI PubMed
6. Kim A, Kim SH, Kim HJ, Yang HK, Hwang JM, Kim JS. Ophthalmoplegia as a complication of cosmetic facial filler injection. *Acta Ophthalmol* 2016;94:e377-9. DOI PubMed
7. Beleznay K, Humphrey S, Carruthers JDA, Carruthers A. Vascular compromise from soft tissue augmentation: experience with 12 cases and recommendations for optimal outcomes. *J Clin Aesthet Dermatol* 2014;7:37-43. PubMed PMC
8. Chatrath V, Banerjee PS, Goodman GJ, Rahman E. Soft-tissue filler-associated blindness: a systematic review of case reports and case series. *Plast Reconstr Surg Glob Open* 2019;7:e2173. DOI PubMed PMC
9. Kim YJ, Choi KS. Bilateral blindness after filler injection. *Plast Reconstr Surg* 2013;131:298e-9e. DOI PubMed
10. Oranges CM, Brucato D, Schaefer DJ, Kalbermatten DF, Harder Y. Complications of nonpermanent facial fillers: a systematic review. *Plast Reconstr Surg Glob Open* 2021;9:e3851. DOI PubMed PMC
11. Beleznay K, Carruthers JD, Humphrey S, Jones D. Avoiding and treating blindness from fillers: a review of the world literature. *Dermatol Surg* 2015;41:1097-117. DOI PubMed
12. Rohrich RJ, Bartlett EL, Dayan E. Practical approach and safety of hyaluronic acid fillers. *Plast Reconstr Surg Glob Open* 2019;7:e2172. DOI PubMed PMC
13. van Loghem J, Funt D, Pavicic T, et al. Managing intravascular complications following treatment with calcium hydroxylapatite: an expert consensus. *J Cosmet Dermatol* 2020;19:2845-58. DOI PubMed PMC
14. Goodman GJ, Magnusson MR, Callan P, et al. A consensus on minimizing the risk of hyaluronic acid embolic visual loss and

suggestions for immediate bedside management. *Aesthet Surg J* 2020;40:1009-21. DOI PubMed PMC

15. DeLorenzi C. Complications of injectable fillers, part 2: vascular complications. *Aesthet Surg J* 2014;34:584-600. DOI PubMed
16. Ten B, Kara T, Kaya Tİ, et al. Evaluation of facial artery course variations and depth by Doppler ultrasonography. *J Cosmet Dermatol* 2021;20:2247-58. DOI PubMed
17. Tseng FW, Bommareddy K, Frank K, et al. Descriptive analysis of 213 positive blood aspiration cases when injecting facial soft tissue fillers. *Aesthet Surg J* 2021;41:616-24. DOI PubMed
18. Lee JG, Yang HM, Hu KS, et al. Frontal branch of the superficial temporal artery: anatomical study and clinical implications regarding injectable treatments. *Surg Radiol Anat* 2015;37:61-8. DOI PubMed
19. Maio M, DeBoulle K, Braz A, Rohrich RJ; Alliance for the Future of Aesthetics Consensus Committee. Facial assessment and injection guide for botulinum toxin and injectable hyaluronic acid fillers: focus on the midface. *Plast Reconstr Surg* 2017;140:540e-50e. DOI PubMed
20. Hufschmidt K, Bronsard N, Foissac R, et al. The infraorbital artery: clinical relevance in esthetic medicine and identification of danger zones of the midface. *J Plast Reconstr Aesthet Surg* 2019;72:131-6. DOI PubMed
21. Zhang-Nunes S, Ryu C, Cahill K, et al. Prospective in vivo evaluation of three different hyaluronic acid gels to varying doses of hyaluronidase with long-term follow-up. *J Plast Reconstr Aesthet Surg* 2021;74:874-80. DOI PubMed
22. Ryu C, Lu JE, Zhang-Nunes S. Response of twelve different hyaluronic acid gels to varying doses of recombinant human hyaluronidase. *J Plast Reconstr Aesthet Surg* 2021;74:881-9. DOI PubMed
23. Zhang-Nunes S, Mehta P, Ryu C, Zhou Q. Response of five different hyaluronic acid gels to varying doses of recombinant human hyaluronidase. In: American Society of Ophthalmic Plastic & Reconstructive Surgery Spring Meeting 2022. Available from: https://asoprsconf.memberclicks.net/assets/docs/ASOPRS_2022_Spring_Program.pdf [Last accessed on 1 Sep 2022].
24. Vrcek IM, Malouf P, Gilliland GD. A novel solution for superficially placed calcium hydroxylapatite (Radiesse) in the inferior eyelid. *Orbit* 2012;31:431-2. DOI PubMed
25. Vu PQ, Grob SR, Tao JP. Light perception vision recovery after treatment for calcium hydroxylapatite cosmetic filler-induced blindness. *Ophthalmic Plast Reconstr Surg* 2018;34:e189-92. DOI PubMed
26. Danysz W, Nowag B, Hengl T, et al. Can sodium thiosulfate act as a reversal agent for calcium hydroxylapatite filler? *Clin Cosmet Investig Dermatol* 2020;13:1059-73. DOI PubMed PMC
27. Rivkin AZ. Volume correction in the aging hand: role of dermal fillers. *Clin Cosmet Investig Dermatol* 2016;9:225-32. DOI PubMed PMC
28. Aguilera SB, Aristizabal M, Reed A. Successful treatment of calcium hydroxylapatite nodules with intralesional 5-fluorouracil, dexamethasone, and triamcinolone. *J Drugs Dermatol* 2016;15:1142-3. PubMed
29. Kapoor KM, Kapoor P, Heydenrych I, Bertossi D. Vision loss associated with hyaluronic acid fillers: a systematic review of literature. *Aesthetic Plast Surg* 2020;44:929-44. DOI PubMed
30. Sito G, Manzoni V, Sommariva R. Vascular complications after facial filler injection: a literature review and meta-analysis. *J Clin Aesthet Dermatol* 2019;12:E65-E72. PubMed PMC
31. Samizadeh S, Pirayesh A, Bertossi D. Anatomical variations in the course of labial arteries: a literature review. *Aesthet Surg J* 2019;39:1225-35. DOI PubMed
32. Toure G, Nguyen TM, Vlavonou S, Ndiaye MM. Transverse facial artery: its role in blindness after cosmetic filler and botulinum toxin injections. *J Plast Reconstr Aesthet Surg* 2021;74:1862-9. DOI PubMed
33. Tansatit T, Phumyoo T, Jitaree B, Sawatwong W, Sahraoui YME. Investigation of the presence and variation of the ascending mental artery: Conventional dissections and ultrasonographic study. *J Cosmet Dermatol* 2019;18:1821-9. DOI PubMed
34. Myung Y, Yim S, Jeong JH, et al. The classification and prognosis of periocular complications related to blindness following cosmetic filler injection. *Plast Reconstr Surg* 2017;140:61-4. DOI PubMed
35. Coleman SR. Avoidance of arterial occlusion from injection of soft tissue fillers. *Aesthet Surg J* 2002;22:555-7. DOI PubMed
36. Carruthers JDA, Fagien S, Rohrich RJ, Weinkle S, Carruthers A. Blindness caused by cosmetic filler injection: a review of cause and therapy. *Plast Reconstr Surg* 2014;134:1197-201. DOI PubMed
37. Cho KH, Dalla Pozza E, Toth G, Bassiri Gharb B, Zins JE. Pathophysiology study of filler-induced blindness. *Aesthet Surg J* 2019;39:96-106. DOI PubMed
38. Tran AQ, Lee WW. vision loss and blindness following fillers. *J dermatology Ski Sci* 2021;3:1-4. PubMed PMC
39. Sorensen EP, Council ML. Update in soft-tissue filler-associated blindness. *Dermatol Surg* 2020;46:671-7. DOI PubMed
40. Ugradar S, Diniz S, Hoenig J, Goldberg RA. Generation of filler emboli as a mechanism for filler-related blindness. *Dermatol Surg* 2021;47:235-7. DOI PubMed
41. Ramesh S, Le A, Katsev B, Ugradar S. The force required to inject a column of filler through facial arteries. *Dermatol Surg* 2020;46:e32-7. DOI PubMed
42. Khan TT, Colon-Acevedo B, Mettu P, DeLorenzi C, Woodward JA. An anatomical analysis of the supratrochlear artery: considerations in facial filler injections and preventing vision loss. *Aesthet Surg J* 2017;37:203-8. DOI PubMed
43. Karam EZ, Gan A, Muci Mendoza R, Martinez E, Perez E. Visual loss after platelet-rich plasma injection into the face. *Neuroophthalmology* 2020;44:371-8. DOI PubMed PMC
44. Roberts SA, Arthurs BP. Severe visual loss and orbital infarction following periorbital aesthetic poly-(L)-lactic acid (PLLA) injection. *Ophthalmic Plast Reconstr Surg* 2012;28:e68-70. DOI PubMed

45. Hayreh SS, Weingeist TA. Experimental occlusion of the central artery of the retina. IV: retinal tolerance time to acute ischaemia. *Br J Ophthalmol* 1980;64:818-25. DOI PubMed PMC
46. Tobalem S, Schutz JS, Chronopoulos A. Central retinal artery occlusion - rethinking retinal survival time. *BMC Ophthalmol* 2018;18:101. DOI PubMed PMC
47. Graue G, Ochoa Araujo DA, Plata Palazuelos C, et al. The M.A.STE.R.S algorithm for acute visual loss management after facial filler injection. *J Cosmet Dermatol* 2020;19:2859-66. DOI PubMed
48. Paap MK, Milman T, Ugradar S, Goldberg R, Silkiss RZ. Examining the role of retrobulbar hyaluronidase in reversing filler-induced blindness: a systematic Review. *Ophthalmic Plast Reconstr Surg* 2020;36:231-8. DOI PubMed
49. Heydenrych I, De Boulle K, Kapoor KM, Bertossi D. The 10-point plan 2021: updated concepts for improved procedural safety during facial filler treatments. *Clin Cosmet Investig Dermatol* 2021;14:779-814. DOI PubMed PMC
50. Butler FK Jr, Hagan C, Murphy-Lavoie H. Hyperbaric oxygen therapy and the eye. *Undersea Hyperb Med* 2008;35:333-87. PubMed
51. Hwang CJ, Morgan PV, Pimentel A, Sayre JW, Goldberg RA, Duckwiler G. Rethinking the role of nitroglycerin ointment in ischemic vascular filler complications: an animal model with ICG imaging. *Ophthalmic Plast Reconstr Surg* 2016;32:118-22. DOI PubMed
52. Shah J. Hyperbaric oxygen therapy. *J Am Col Certif Wound Spec* 2010;2:9-13. DOI PubMed PMC
53. Uittenbogaard D, Lansdorp CA, Bauland CG, Boonstra O. Hyperbaric oxygen therapy for dermal ischemia after dermal filler injection with calcium hydroxylapatite: a case report. *Undersea Hyperb Med* 2019;46:207-10. PubMed
54. Hung JH, Wang CT, Lee CN, Shieh SJ. Unilateral vision loss after hyaluronic acid injection: a case report. *Ann Plast Surg* 2021;86:S127-31. DOI PubMed
55. Wu CW, Wu HJ. Retinal artery occlusion following cosmetic injection of poly-L-lactic acid. *Taiwan J Ophthalmol* 2021;11:317-20. DOI PubMed PMC
56. Hu XZ, Hu JY, Wu PS, Yu SB, Kikkawa DO, Lu W. Posterior ciliary artery occlusion caused by hyaluronic acid injections into the forehead: a case report. *Medicine (Baltimore)* 2016;95:e3124. DOI PubMed PMC
57. Celebi ARC, Kilavuzoglu AE, Altiparmak UE, Cosar CB, Ozkiris A. Hyperbaric oxygen for the treatment of the rare combination of central retinal vein occlusion and cilioretinal artery occlusion. *Diving Hyperb Med* 2016;46:50-3. PubMed
58. Kim YS, Nam MS, Park EJ, et al. The effect of adjunctive hyperbaric oxygen therapy in patients with central retinal artery occlusion. *Undersea Hyperb Med* 2020;47:57-64. PubMed
59. Kim SH, Cha YS, Lee Y, Kim H, Yoon IN. Successful treatment of central retinal artery occlusion using hyperbaric oxygen therapy. *Clin Exp Emerg Med* 2018;5:278-81. DOI PubMed PMC
60. Lemos JA, Teixeira C, Carvalho R, Fernandes T. Combined central retinal artery and vein occlusion associated with factor V leiden mutation and treated with hyperbaric oxygen. *Case Rep Ophthalmol* 2015;6:462-8. DOI PubMed PMC
61. Chesnut C. Restoration of visual loss with retrobulbar hyaluronidase injection after hyaluronic acid filler. *Dermatol Surg* 2018;44:435-7. DOI PubMed
62. Wibowo A, Kapoor KM, Philipp-Dormston WG. Reversal of post-filler vision loss and skin ischaemia with high-dose pulsed hyaluronidase injections. *Aesthetic Plast Surg* 2019;43:1337-44. DOI PubMed
63. Thanasarnaksorn W, Cotofana S, Rudolph C, Kraisak P, Chanasumon N, Suwanchinda A. Severe vision loss caused by cosmetic filler augmentation: case series with review of cause and therapy. *J Cosmet Dermatol* 2018;17:712-8. DOI PubMed
64. Zhu GZ, Sun ZS, Liao WX, et al. Efficacy of retrobulbar hyaluronidase injection for vision loss resulting from hyaluronic acid filler embolization. *Aesthet Surg J* 2017;38:12-22. DOI PubMed
65. Zhang L, Feng X, Shi H, Wu WTL, Wu S. Blindness after facial filler injections: the role of extravascular hyaluronidase on intravascular hyaluronic acid embolism in the rabbit experimental model. *Aesthet Surg J* 2020;40:319-26. DOI PubMed
66. Hwang CJ, Mustak H, Gupta AA, Ramos RM, Goldberg RA, Duckwiler GR. Role of retrobulbar hyaluronidase in filler-associated blindness: evaluation of fundus perfusion and electroretinogram readings in an animal model. *Ophthalmic Plast Reconstr Surg* 2019;35:33-7. DOI PubMed
67. Lee W, Oh W, Ko HS, Lee SY, Kim KW, Yang EJ. Effectiveness of retrobulbar hyaluronidase injection in an iatrogenic blindness rabbit model using hyaluronic acid filler injection. *Plast Reconstr Surg* 2019;144:137-43. DOI PubMed
68. Hwang CJ, Perry JD. Effectiveness of retrobulbar hyaluronidase injection in an iatrogenic blindness rabbit model using hyaluronic acid filler injection. *Plast Reconstr Surg* 2020;145:658e-60e. DOI PubMed
69. Paap MK, Milman T, Ugradar S, Silkiss RZ. Assessing retrobulbar hyaluronidase as a treatment for filler-induced blindness in a cadaver model. *Plast Reconstr Surg* 2019;144:315-20. DOI PubMed
70. Ugradar S. Quantifying the digestion of cross-linked hyaluronic acid fillers with hyaluronidase. *Dermatol Surg* 2021;47:1233-6. DOI PubMed
71. Burns PB, Rohrich RJ, Chung KC. The levels of evidence and their role in evidence-based medicine. *Plast Reconstr Surg* 2011;128:305-10. DOI PubMed PMC
72. Baley-Spindel I, Villaseñor-Villalpando E, Márquez-Espriella C, Rivera-Salgado MI, Dávila-Díaz R. Perivascular hyaluronidase with alteplase as treatment for hyaluronic acid thrombosis. *Aesthet Surg J* 2020;40:551-9. DOI PubMed
73. Park KH, Kim YK, Woo SJ, et al; Korean Retina Society. Iatrogenic occlusion of the ophthalmic artery after cosmetic facial filler injections: a national survey by the Korean Retina Society. *JAMA Ophthalmol* 2014;132:714-23. DOI PubMed
74. Yang HK, Lee Y, Woo SJ, Park KH, Kim JS, Hwang JM. Natural course of ophthalmoplegia after iatrogenic ophthalmic artery

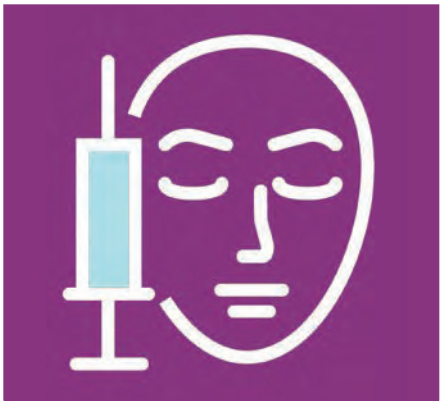
occlusion caused by cosmetic filler injections. *Plast Reconstr Surg* 2019;144:28e-34e. DOI PubMed

75. Zimmerman CF, Van Patters PD, Golnik KC, Kopitnik TA, Anand R. Orbital infarction syndrome after surgery for intracranial aneurysms. *Ophthalmology* 1995;102:594-8. DOI PubMed
76. Downie EM, Chen Y, Lucarelli MJ, Burkat CN. Isolated ophthalmoplegia following filler injections to the upper face. *Ophthalmic Plast Reconstr Surg* 2020;36:e152-4. DOI PubMed PMC
77. Bae IH, Kim MS, Choi H, Na CH, Shin BS. Ischemic oculomotor nerve palsy due to hyaluronic acid filler injection. *J Cosmet Dermatol* 2018;17:1016-8. DOI PubMed
78. Sclafani AP, Fagien S. Treatment of injectable soft tissue filler complications. *Dermatol Surg* 2009;35 Suppl 2:1672-80. DOI PubMed
79. Loh KTD, Phoon YS, Phua V, Kapoor KM. Successfully managing impending skin necrosis following hyaluronic acid filler injection, using high-dose pulsed hyaluronidase. *Plast Reconstr Surg Glob Open* 2018;6:e1639. DOI PubMed PMC
80. Boulle K, Heydenrych I. Patient factors influencing dermal filler complications: prevention, assessment, and treatment. *Clin Cosmet Investig Dermatol* 2015;8:205-14. DOI PubMed PMC
81. Goodman GJ, Roberts S, Callan P. Experience and management of intravascular injection with facial fillers: results of a multinational survey of experienced injectors. *Aesthetic Plast Surg* 2016;40:549-55. DOI PubMed
82. Silva MT, Curi AL. Blindness and total ophthalmoplegia after aesthetic polymethylmethacrylate injection: case report. *Arq Neuropsiquiatr* 2004;62:873-4. DOI PubMed
83. Figueiredo JC, Naufal RR, Zampar AG, Mélega JM. Expanded median forehead flap and abbé flap for nasal and upper lip reconstruction after complications of polymethylmethacrylate. *Aesthetic Plast Surg* 2010;34:385-7. DOI PubMed
84. Cohen JL. Understanding, avoiding, and managing dermal filler complications. *Dermatol Surg* 2008;34 Suppl 1:S92-9. DOI PubMed
85. Ortiz AE, Ahluwalia J, Song SS, Avram MM. Analysis of U.S. food and drug administration data on soft-tissue filler complications. *Dermatol Surg* 2020;46:958-61. DOI PubMed
86. Tansatit T, Apinuntrum P, Phetudom T. Facing the worst risk: confronting the dorsal nasal artery, implication for non-surgical procedures of nasal augmentation. *Aesthetic Plast Surg* 2017;41:191-8. DOI PubMed
87. Rauso R, Bove P, Rugge L, Chirico F. Unusual intraoral necrosis after hyaluronic acid injections. *Dermatol Surg* 2021;47:1158-60. DOI PubMed
88. Chuchvara N, Alamgir M, John AM, Rao B. Dermal filler-induced vascular occlusion successfully treated with tadalafil, hyaluronidase, and aspirin. *Dermatol Surg* 2021;47:1160-2. DOI PubMed
89. Tansatit T, Phumyoo T, MCCabe H, Jitaree B. Translucent and ultrasonographic studies of the inferior labial artery for improvement of filler injection techniques. *Plast Reconstr Surg Glob Open* 2019;7:e2399. DOI PubMed PMC
90. Wang Q, Zhao Y, Li H, Li P, Wang J. Vascular complications after chin augmentation using hyaluronic acid. *Aesthetic Plast Surg* 2018;42:553-9. DOI PubMed
91. Fang M, Rahman E, Kapoor KM. Managing complications of submental artery involvement after hyaluronic acid filler injection in chin region. *Plast Reconstr Surg Glob Open* 2018;6:e1789. DOI PubMed PMC
92. Murray G, Convery C, Walker L, Davies E. Guideline for the management of hyaluronic acid filler-induced vascular occlusion. *J Clin Aesthet Dermatol* 2021;14:E61-9. PubMed PMC
93. Dayan SH. Complications from toxins and fillers in the dermatology clinic: recognition, prevention, and treatment. *Facial Plast Surg Clin North Am* 2013;21:663-73. DOI PubMed
94. Darling MD, Peterson JD, Fabi SG. Impending necrosis after injection of hyaluronic acid and calcium hydroxylapatite fillers: report of 2 cases treated with hyperbaric oxygen therapy. *Dermatol Surg* 2014;40:1049-52. DOI PubMed
95. Avci P, Gupta A, Sadasivam M, Vecchio D, Pam Z, Pam N, Hamblin MR. Low-level laser (light) therapy (LLLT) in skin: stimulating, healing, restoring. *Semin Cutan Med Surg* 2013;32:41-52. PubMed PMC
96. Nishioka MA, Pinfildi CE, Sheliga TR, Arias VE, Gomes HC, Ferreira LM. LED (660 nm) and laser (670 nm) use on skin flap viability: angiogenesis and mast cells on transition line. *Lasers Med Sci* 2012;27:1045-50. DOI PubMed
97. Beer K, Downie J, Beer J. A treatment protocol for vascular occlusion from particulate soft tissue augmentation. *J Clin Aesthet Dermatol* 2012;5:44-7. PubMed PMC
98. Oley MH, Oley MC, Mawu FO, Aling DMR, Faruk M. Hyperbaric oxygen therapy in managing minimally invasive aesthetic procedure complications: a report of three cases. *Clin Cosmet Investig Dermatol* 2022;15:63-8. DOI PubMed PMC
99. Henderson R, Reilly DA, Cooper JS. Hyperbaric oxygen for ischemia due to injection of cosmetic fillers: case report and issues. *Plast Reconstr Surg Glob Open* 2018;6:e1618. DOI PubMed PMC
100. DeLorenzi C. New high dose pulsed hyaluronidase protocol for hyaluronic acid filler vascular adverse events. *Aesthet Surg J* 2017;37:814-25. DOI PubMed
101. Ansari ZA, Choi CJ, Rong AJ, Erickson BP, Tse DT. Ocular and cerebral infarction from periocular filler injection. *Orbit* 2019;38:322-4. DOI PubMed
102. Lee JS, Kim JY, Woo SJ. Unilateral blindness with bilateral brain infarction after cosmetic facial filler injection. *J Neuroophthalmol* 2021;41:e566-71. DOI PubMed
103. Yang Q, Lu B, Guo N, et al. Fatal cerebral infarction and ophthalmic artery occlusion after nasal augmentation with hyaluronic acid-a case report and review of literature. *Aesthetic Plast Surg* 2020;44:543-8. DOI PubMed

ATTACHMENT D

104. Lee W, Koh IS, Oh W, Yang EJ. Ocular complications of soft tissue filler injections: A review of literature. *J Cosmet Dermatol* 2020;19:772-81. DOI PubMed
105. Ozturk CN, Li Y, Tung R, Parker L, Piliang MP, Zins JE. Complications following injection of soft-tissue fillers. *Aesthet Surg J* 2013;33:862-77. DOI PubMed
106. Alam M, Kakar R, Dover JS, et al. Rates of vascular occlusion associated with using needles vs. cannulas for filler injection. *JAMA Dermatol* 2021;157:174-80. DOI PubMed PMC
107. Ugradar S, Hoenig J. Measurement of the force required by blunt-tipped microcannulas to perforate the facial artery. *Ophthalmic Plast Reconstr Surg* 2019;35:444-6. DOI PubMed
108. Halepas S, Peters SM, Goldsmith JL, Ferneini EM. Vascular compromise after soft tissue facial fillers: case report and review of current treatment protocols. *J Oral Maxillofac Surg* 2020;78:440-5. DOI PubMed
109. Lee W, Kim JS, Moon HJ, Yang EJ. A safe doppler ultrasound-guided method for nasolabial fold correction with hyaluronic acid filler. *Aesthet Surg J* 2021;41:NP486-92. DOI PubMed
110. Mespreuve M, Waked K, Hendrickx B. Visualization techniques of the facial arteries. *J Cosmet Dermatol* 2021;20:386-90. DOI PubMed PMC
111. Rocha PS, Guerra TA, Teixeira DA. Description of a safe doppler ultrasound-guided technique for hyaluronic acid filler in the face-A method to avoid adverse vascular events. *J Cosmet Dermatol* 2022;21:2783-7. DOI PubMed
112. Schelke LW, Decates TS, Velthuis PJ. Ultrasound to improve the safety of hyaluronic acid filler treatments. *J Cosmet Dermatol* 2018;17:1019-24. DOI PubMed
113. Lee AL, Chen YF, Yao WT, et al. Laser doppler imaging for treating vascular complications from procedures involving dermal fillers: case series and literature review. *Diagnostics (Basel)* 2021;11:1640. DOI PubMed PMC
114. Huang P, Liu A, Ren H, Xue K. Color doppler flow imaging of retrobulbar ocular blood flow changes in retinal artery occlusions caused by cosmetic facial filler injections. *Ophthalmic Plast Reconstr Surg* 2019;35:227-31. DOI PubMed
115. AlGhadeer H, Talea M, Al-Muhaylib A, AlSheikh O, Elkhamary SM. Acute unilateral vision loss and bilateral cerebral infarction following cosmetic filler injection. *Orbit* 2021. DOI PubMed
116. Mundada P, Kohler R, Boudabbous S, Toutous Trellu L, Platon A, Becker M. Injectable facial fillers: imaging features, complications, and diagnostic pitfalls at MRI and PET CT. *Insights Imaging* 2017;8:557-72. DOI PubMed PMC
117. Davidova P, Müller M, Wenner Y, König C, Kenikstul N, Kohnen T. Ophthalmic artery occlusion after glabellar hyaluronic acid filler injection. *Am J Ophthalmol Case Rep* 2022;26:101407. DOI PubMed PMC
118. Danks JJ, Dalgliesh JD, Ayton T. Cosmetic filler blindness: recovery after repeated hyaluronidase injections. *Aesthet Surg J* 2022;42:411-6. DOI PubMed
119. Nguyen HH, Tran HTT, Duong QH, Nguyen MD, Dao HX, Le DT. Significant vision recovery from filler-induced complete blindness with combined intra-arterial injection of hyaluronidase and thrombolytic agents. *Aesthetic Plast Surg* 2022;46:907-11. DOI PubMed
120. Moore RM, Mueller MA, Hu AC, Evans GRD. Asymptomatic stroke after hyaluronic acid filler injection: case report and literature review. *Aesthet Surg J* 2021;41:NP602-8. DOI PubMed
121. Eldweik L. Orbital infarction syndrome following hyaluronic acid filler rhinoplasty. *Am J Ophthalmol Case Rep* 2021;22:101063. DOI PubMed PMC
122. Jolly R, Bhalla M, Zakir R, Joshi N. Visual loss from dermal fillers. *Eur J Ophthalmol* 2021;31:NP102-5. DOI PubMed
123. Zhang L, Luo Z, Li J, et al. Endovascular hyaluronidase application through superselective angiography to rescue blindness caused by hyaluronic acid injection. *Aesthet Surg J* 2021;41:344-55. DOI PubMed
124. Liu H, Chen D, Zhang J. Ophthalmic artery occlusion after forehead autologous fat injection. *Retin Cases Brief Rep* 2020;14:271-4. DOI PubMed
125. Conovaloff J, Hrachova M, Hasso A, Abcede H. Vanishing beauty: a case of a 59-year-old woman with iatrogenic central retinal artery occlusion after cosmetic facial augmentation with filler injections (2694). *Neurology* 2020:94(15 Supplement). DOI
126. Ramesh S, Fiaschetti D, Goldberg RA. Orbital and ocular ischemic syndrome with blindness after facial filler injection. *Ophthalmic Plast Reconstr Surg* 2018;34:e108-10. DOI PubMed
127. Chen H, Wang H, Yang Z. A case of hyaluronic acid induced blindness with ophthalmoplegia and ptosis. *Ophthalmic Plast Reconstr Surg* 2018;34:e184-6. DOI PubMed
128. Kalyam K, Kavoussi SC, Ehrlich M, et al. Irreversible blindness following periocular autologous platelet-rich plasma skin rejuvenation treatment. *Ophthalmic Plast Reconstr Surg* 2017;33:S12-6. DOI PubMed

ATTACHMENT D



META-ANALYSIS

Vascular Complications after Facial Filler Injection:

A Literature Review and Meta-analysis

by GIUSEPPE SITO, MD, PhD; VERONICA MANZONI, MD; and RAFFAELLA SOMMARIVA, MD

Prof. Sito is with the Prof. Professor Giuseppe Sito Clinic in Turin, Italy. Dr. Manzoni is with the Istituto Auxologico Italiano in Milan, Italy. Dr. Sommariva is a specialist in plastic surgery practicing in Acqui Terme, Italy and Genoa, Italy.

J Clin Aesthet Dermatol. 2019;12(6):E65–E72

ABSTRACT

Background: Vascular occlusion during the injection of facial fillers is uncommon, but can result in serious adverse events, including necrosis, blindness, and stroke. **Objectives:** We explored factors that influence the frequency and severity of vascular complications during filler injections. **Methods:** This was a meta-analysis that included case reports and case series published during the years 2004 to 2016 describing patients who experienced any type of vascular complication after an aesthetic procedure. In addition to the descriptive analysis of the variables retrieved, a logistic regression for predicting the outcome of the vascular event was performed. **Results:** The analysis included 93 cases described in 30 articles. Blindness was the main consequence of the vascular complications (n=57; 61%). The reported outcome was partial or total recovery in 24 cases (28%) and no improvement in 61 cases (72%). Hyaluronic acid (HA) and autologous fat were the two fillers most frequently involved in vascular occlusions, with autologous fat showing a stronger trend toward no improvement than HA. Involvement of the ophthalmic and retinal arteries was most frequently associated with no improvement.**Conclusion:** Injury to ophthalmic and retinal arteries during the injection of facial fillers can result in irreversible serious adverse events. Physicians performing facial filler injections should have a proficient knowledge of anatomy.

KEYWORDS: Dermal fillers, vascular complications, hyaluronic acid, autologous fat, collagen, adverse events

Nonsurgical cosmetic procedures are a growing trend worldwide. Included among these minimally invasive techniques are botulinum toxin and soft-tissue augmentation with fillers, which are used restore tissue loss and correct aging-related rhytides and folds. In 2011, dermal fillers were used in nearly 1.6 million aesthetic procedures, increasing to 2.3 million in 2013 and 5.5 million in 2014.[1–3]

Hyaluronic acid (HA) fillers are the most commonly used injectable fillers, followed by autologous fat. According to the American Society for Aesthetic Plastic Surgery, nearly 900,000 soft-tissue augmentation procedures were performed with HA in 2004.[4,5] Other commonly used filler materials include bovine and human collagen (active for 1–3 months before degradation); poly-L-lactic acid, which stimulates endogenous collagen production for up to 15 months; and calcium hydroxylapatite, which offers up to 2 years of activity.[3] These fillers can all be used for volume replacement and enhancement, such as cheek and chin augmentation, tear trough valley correction, nose reshaping (rhinoplasty), midface volumization, and lip enhancement.[1,5–7] Although these procedures are generally considered safe, some local adverse events, aside from the relatively common site-injection reactions (e.g., swelling, tenderness, pain, bruising), have been observed.[8–10] These include edema, erythema, scarring, granuloma formation, hyper- and hypopigmentation, infection, abscess formation, herpetic outbreaks, nodular masses, and paresthesia (if a nerve has been pinched during the procedure). While these adverse reactions are usually transient, the common use of three-dimensional facial volume restoration techniques, where the filler material can be injected at any depth, has brought about infrequent but serious and often irreversible vascular complications caused by symptomatic arterial occlusion.[6,11–13] These vascular complications can result in persistent skin necrosis, ophthalmoplegia, permanent unilateral or bilateral vision loss, and stroke.[11–13] Ocular and cerebral embolism occurs when the injected material travels from the distal to proximal retinal and ophthalmic arteries, causing sudden, excruciating pain, persistent blindness, and further tissue necrosis.[11–13] In addition to fillers accessing the vessel lumen, vascular occlusion can occur by external compression of the stiff gel bolus deposited in direct contact with the vessel wall.[14–16]

Based on the available literature, some authors have suggested that the injection technique, site, and substance can have significant influence on the level of risk for an adverse vascular event.[2,5,7,11,12,17] However, most of these reviews were not systematic, and the potential influence of other variables on the incidence of adverse events has not been addressed. Therefore, we reviewed the literature regarding vascular

FUNDING: No funding was provided for this study.
DISCLOSURES: The authors have no conflicts of interest relevant to the content of this article.
CORRESPONDENCE: Prof. Giuseppe Sito; Email: mail@giuseppesito.it

complications and performed a meta-analysis of the variables that potentially affect the frequency and severity of adverse events.

METHODS

Literature search and article selection.

This meta-analysis included data from case reports and case series of patients experiencing any type of vascular complication after an aesthetic procedure published during the years 2004 to 2016. The main source for article retrieval was the PubMed. Additional sources included Google Scholar, where the search was restricted to the article title, and a case series by Park et al,[18] which provided details from 19 cases previously published as case reports. The database search, performed on December 2016, combined the term *filler* with the following terms: *injection* (or *injected*), *blindness*, *visual loss*, *ophthalmoplegia*, *artery occlusion*, *embolism*, *ischemia* (or *ischemic*), *necrosis*, and *complication*. Only full-text articles written in English were considered for eligibility. To be included in the analysis, cases had to report a vascular event occurring after an aesthetic procedure on the human face.

Data extraction and management.

Data for the meta-analysis were extracted from each case and transferred to a predefined form containing the following variables: case reference, age, sex, injected product, aesthetic procedure, needle diameter, injected volume, person who injected the product, injection site, blood vessel affected, main consequence(s) of the vascular event, concomitant symptoms, time to symptom onset, intervention performed to treat the vascular complication, and outcome. Additionally, diagnostic tests performed to confirm the occurrence of vascular complications were recorded to address the quality of the articles included in our review. The main consequences of a vascular complication were blindness, visual loss, necrosis, and other. Blindness was only considered when explicitly stated in the text, whereas visual loss included a reduction in visual acuity, the perception of light only, and the perception of hand movement only. Time-to-onset values were grouped into three categories: less than one hour postprocedure, 1 to 24 hours postprocedure, and more than 24 hours postprocedure. The final outcome was categorized as no change, partial recovery, or full recovery based on the progress of the main consequence of the vascular complication.

TABLE 1. Characteristics of cases included in the meta-analysis

CHARACTERISTIC		n	%*
Sex (n=93)	Female	84	90.3
	Male	9	9.7
Injected substance (n=92)	Hyaluronic acid	40	43.5
	Autologous fat	38	41.3
	Collagen	7	7.6
	Calcium hydroxylapatite	4	4.3
	Poly-(L)-lactic acid	3	3.3
Injection site** (n=90)	Glabella	44	48.9
	Nose	41	45.6
	Periocular	9	9.7
	Frontal/temple area	11	12.2
Affected blood vessel (n=82)	Ophthalmic artery	36	43.9
	Central retinal artery	29	35.4
	Nasociliary artery	8	9.8
	Other	9	11.0
Main consequence** (n=93)	Blindness	57	61.3
	Visual loss	21	22.6
	Skin necrosis	11	11.8
Concomitant symptoms** (n=68)	Pain	32	47.1
	Erythema	3	4.4
	Ptosis	31	45.6
	Edema	11	16.2
Imaging diagnostic tests** (n=80)	Angiography	31	38.8
	OCT	4	5.0
	MRI	52	65.0
	Fundus imaging	15	18.8
	Ultrasonography	1	1.3
Time to symptoms onset (n=73)	< 1 hour	13	17.8
	1–24 hours	47	64.4
	> 24 hours	12	16.4
Outcome (n=85)	Total or partial recovery	24	28.2
	No improvement	61	71.8

* Percentages are shown based on available cases
** More than one category can apply to each case

Statistical analysis.

Categorical variables were described as frequency and percentage, whereas quantitative variables were described as means and standard deviations (SDs). To assess the factors possibly influencing the outcome of vascular complications, the percentages of cases with no improvement and those showing partial or full recovery were compared using the chi-squared test. For variables showing statistically significant differences, a *post-hoc* analysis was performed by computing the chi-squared values of the adjusted residuals and applying the Bonferroni correction, as described by Beasley et al.[19] A prediction model (multivariate analysis) for the vascular event outcomes was built using logistic regression. The multivariate analysis included all variables regarding events occurring prior to any vascular complication, which showed

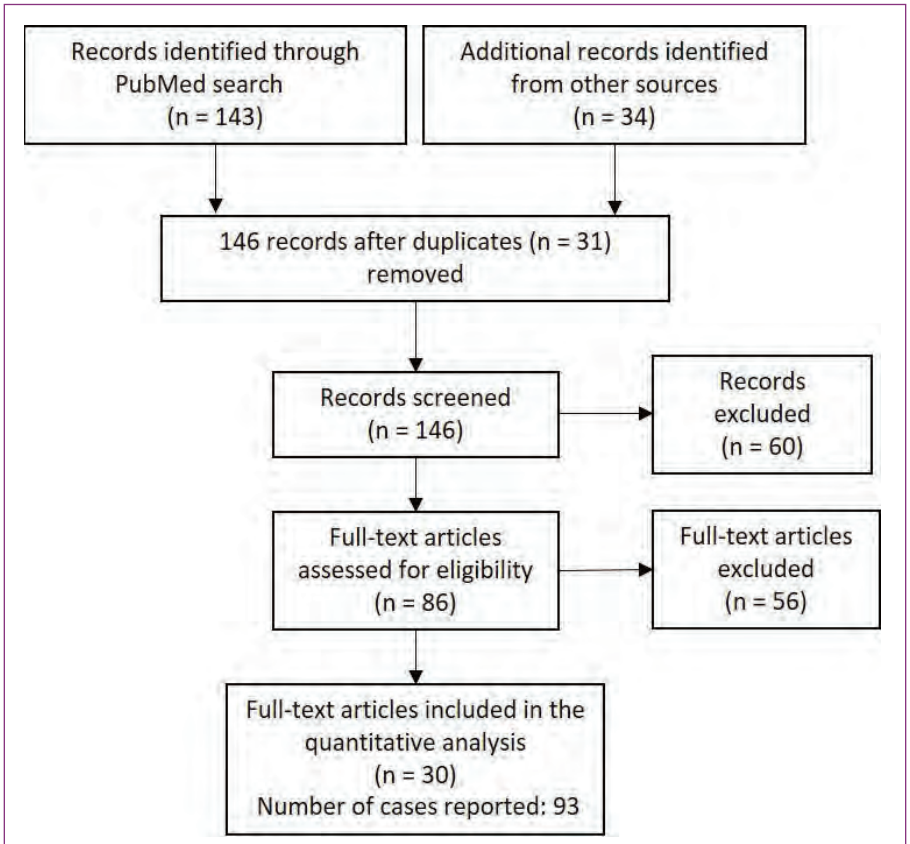


FIGURE 1. Flow diagram of study inclusion.

significant differences when comparing patients without improvement and those with partial or total recovery. The significant threshold was set at α=0.05 and all analyses were performed using the Statistical Package for the Social Sciences version 22.0 for Windows software program (IBM Corp., Armonk, New York).

RESULTS

Study selection. The initial search (including articles retrieved from additional sources) yielded 143 articles, published during the years 2004 to 2016, on vascular events potentially associated with the use of injected fillers (Figure 1). After removing duplicates and excluding non-English articles and those without full-text availability, 86 were considered eligible. Of these, 56 either reported results at injection sites other than the face or did not report any vascular complication, and thus were discarded. The final selection included 30 full-text articles reporting 93 cases: 22 case reports (i.e., articles containing a full description of one or more cases),[2,8,13,20–39] seven case series (i.e., articles containing a tabulated description of various cases with vascular complications),[18,40–44] and one observational trial (i.e., an article retrieving data from a cohort of patients, including at least one patient experiencing a vascular complication).[45] Most cases (n=62; 66.7%) were reported in Korea, while 14 (15.1%) were reported in China, 10 (10.8%) were reported in the United States, three (3.2%) were reported in Germany, three (3.2%) were reported in Taiwan, and one (1.1%) was reported in Japan.

All cases had information regarding the injection site and main consequences of vascular complications. Other key variables, such as injected substance, outcome, and affected blood vessel were reported in 92 (98.9%), 85 (91.4%), and 82 (88.2%) cases, respectively. In 80 cases (86.0%), the vascular complication and identity of the affected blood vessel were confirmed by at least one of the following imaging techniques: optical coherence tomography, magnetic resonance imaging, ultrasonography, or fundoscopy. In six cases, the affected vessel was deduced from the signs (e.g., necrosis affecting a skin area clearly irrigated by the facial artery) or the treatment outcome (e.g., prostaglandins injected into a vein, leading to the improvement of signs and symptoms). Conversely, in four cases, the physician failed to identify the affected vessel despite performing imaging diagnostic tests. Needle diameter, injected volume, and the professional who performed the injection were only reported in 11, 17, and 13 cases, respectively; due to their low representation in the study sample, these variables were excluded from analysis.

Case characteristics. Table 1 summarizes the main characteristics of the cases described in the selected articles. In most cases (n=57; 61.3%), blindness was the main consequence of vascular complication. In five cases (5.4%), the patients experienced blindness and skin necrosis simultaneously. Whereas blindness was typically assumed to be a consequence of a vascular embolization of the filler material, necrosis was sometimes attributed to compression (Figure 2).[2,39,45] However, none of these cases reported evidence regarding the etiology of skin necrosis, and compression was suggested based on the time-to-onset or necrosis progression. Nine patients (9.7%) experienced neither necrosis nor visual loss or blindness despite a diagnosis of vascular occlusion. Eight patients (8.6%) reported mild consequences (e.g., pain, erythema), all of which resolved completely. One patient that was injected with autologous fat in the glabella experienced occlusion of the retinal artery with concomitant brain infarction, which resulted in hemiplegia and death.[43]

Theoretically, multiple blood vessels and nerves can be reached by the needle during filler injection (Figure 3). However, the paths of facial, nasal, temporal, and ophthalmic arteries define anatomical areas with increased risk of injury during filler injection (Figure 4). In the case of the ophthalmic artery, the increased risk included occlusion of one of its most important branches: the retinal artery. In our analysis, the ophthalmic retinal arteries accounted for 79.3 percent of the cases in which the affected blood vessel was reported. In addition to the nasociliary artery, other blood vessels affected by the aesthetic procedure were the choroid vessels, the internal carotid artery, the middle cerebral artery, and the facial vein and artery. The occlusion of the ophthalmic artery was mostly due to injections in the nose (n=18, 42.9% of all cases affecting the ophthalmic artery). Conversely, the occlusion of the retinal artery was mostly due to injections in the

glabella (n=18, 55% of all cases affecting the retinal artery).

In 12 cases (12.9%), vascular occlusion progressed to brain infarction, identified by magnetic resonance imaging. Two of these were associated with ophthalmic artery occlusion, whereas eight were associated with retinal artery occlusion. With the exception of two cases—one leading to the patient's death and another resulting in neurological sequelae—blindness was the main consequence for all patients affected by brain infarction.

Full recovery was reported in seven cases (8.2%): one case of blindness, one of visual loss, and five cases of vascular occlusion with minor consequences. Temporary blindness was caused by an HA injection in the eyebrow. The patient reported foggy and hazy vision immediately after the filler injection; 10 days later, the filler was successfully removed by irrigation and aspiration after creating a temporal limbal incision in the affected eye. Eight days after removal, visual acuity was restored.[27]

Hyaluronidase was used only in 10 of 40 cases in which HA was the cause of vascular occlusion. The time between symptom onset and hyaluronidase injection exceeded three hours in all cases. The dose of hyaluronidase injected, reported only in five cases, ranged from 1,000 to 9,000 units. In five of these cases, blindness was the main consequence of the vascular event; only one patient experienced partial recovery,[25] whereas the rest remained blind despite attempts to remove the HA obstruction by injecting hyaluronidase.

Factors influencing outcome. To explore possible baseline factors influencing the outcome, cases with either visual loss or blindness as the main consequence were grouped into two categories based on the outcome: total or partial recovery and no improvement (Table 2). A chi-squared test revealed significant differences in the injected substance, the affected blood vessel, and the time to symptom onset. The *post-hoc* analysis of the injected substance showed that both HA and autologous fat were significantly associated with no improvement (p=0.003 and p<0.001 for the chi-squared adjusted residuals of HA and autologous fat, respectively; the significance threshold after Bonferroni correction was set at α=0.005). Regarding the affected vessel, only the ophthalmic artery was significantly associated with no improvement (p=0.001 for the chi-squared adjusted residuals; the significant threshold after the Bonferroni correction was set at α=0.006). A *post-hoc* analysis of time-to-onset did not reveal significant differences in any of the three categories.

The injected substance, the affected blood vessel, and the time to symptoms onset were included in a logistic regression analysis. The resulting model explained 22 percent of the outcome's variance, categorized as "no improvement" and "total or partial recovery" (R^2=0.219; p=0.027). However, only the affected blood vessel significantly contributed to the overall model (Table 3).

TABLE 2. Distribution of cases in variables potentially influencing the outcome

VARIABLE		TOTAL OR PARTIAL RECOVERY, n=24 n (%)	NO IMPROVEMENT, n=61 n (%)	*p*-VALUE
Sex	Female	21 (27.6)	55 (72.4)	0.719
	Male	3 (33.3)	6 (66.7)	
Injected substance	Hyaluronic acid	16 (45.7)	19 (54.3)	<0.001
	Autologous fat	1 (2.7)	36 (97.3)	
	Collagen	4 (66.7)	2 (33.3)	
	Calcium hydroxylapatite	3 (75.0)	1 (25.0)	
	Poly-(L)-lactic acid	0	3 (100.0)	
Injection site*	Nose	14 (35.9)	25 (64.1)	0.132
	Glabella	8 (19.0)	34 (81.0)	0.063
	Periocular	1 (16.7)	5 (83.3)	0.519
	Frontal/temple area	3 (30.0)	7 (70.0)	0.883
Affected blood vessel	Ophtalmic artery	2 (5.6)	34 (94.4)	0.004
	Retinal artery	6 (26.1)	17 (73.9)	
	Nasociliary artery	4 (50.0)	4 (50.0)	
	Other	4 (50.0)	4 (50.0)	
Time to onset	<1 hour	5 (41.7)	7 (58.3)	0.024
	1–24 hours	10 (22.2)	35 (77.8)	
	>24 hours	6 (66.7)	3 (33.3)	

*Patients could have more than one injection site

TABLE 3. Individual contribution of variables in the logistic regression to predict the outcome of the vascular complication

VARIABLE	OR (95% CI)	*P*-VALUE
Injected substance	1.3 (0.7–2.5)	0.391
Affected blood vessel	0.4 (0.2–0.8)	0.007
Time to symptom onset	0.8 (0.2–2.6)	0.708

CI: confidence interval; OR: odds ratio

DISCUSSION

In this systematic review and meta-analysis of patients with vascular complications occurring after aesthetic procedures, we found that unilateral blindness was the most frequent vascular adverse event associated with cosmetic fillers for facial tissue augmentation. Of these, autologous fat tended to cause more cases of permanent vascular damage. Among all blood vessels affected, the ophthalmic artery was significantly associated with irreversible blindness.

The risk of vascular complications associated with facial aesthetic procedures has been addressed previously in case reports, case series, and literature reviews. In an attempt to further understand the factors influencing the risks and outcomes of vascular complications, we extracted data from individual cases to provide a quantitative approach. Moreover, considering that the number of products available for soft-tissue augmentation has been progressively and continuously increasing for the last 10 years, our

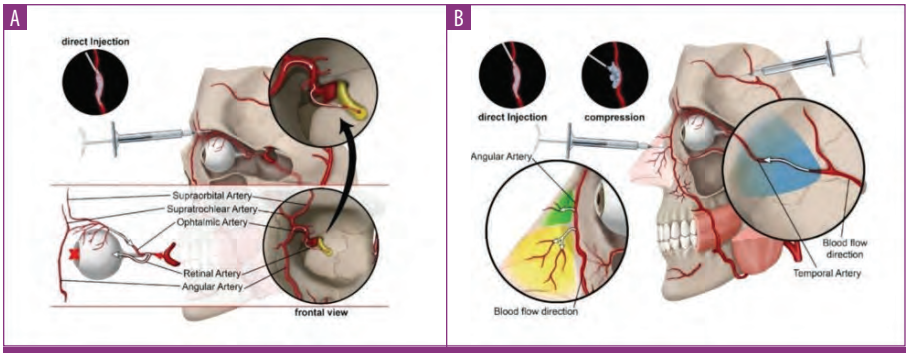


FIGURE 2. Etiological details of blindness caused by A) direct injection of the filler into the vessel lumen and B) skin necrosis caused by either direct injection or vascular compression

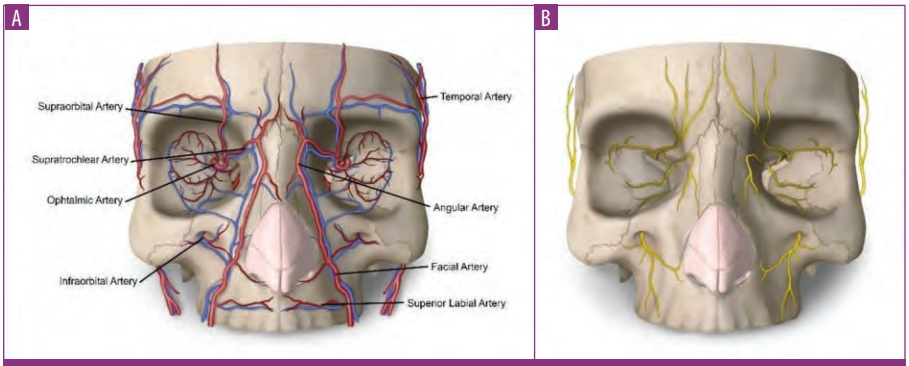


FIGURE 3. A) main vascular and B) nerve structures of the face

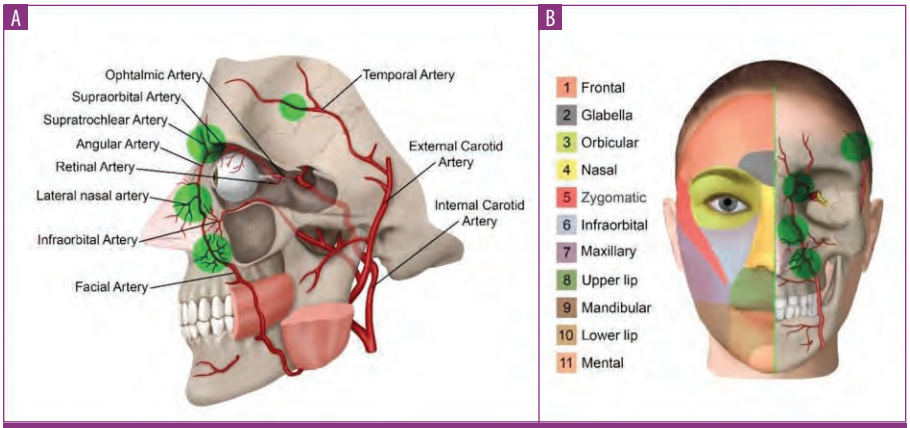


FIGURE 4. A) depiction of facial arteries illustrating the primary areas of risk and B) their associated anatomical structure

review aimed to present an updated picture of vascular complications associated with these fillers. All analyses based on case reports are constrained by the amount and accuracy of the information published. Eighty-six percent of cases reported using imaging diagnostic techniques to verify the diagnosis of vascular occlusion, and most of them provided details regarding key variables such as the injected substance, the blood vessel affected, the outcome of the vascular complication, and the time to symptom onset.

In terms of clinical correlation, one of the most relevant variables was the filler injected. In our study selection, the absolute number of cases with vascular complications after the use of HA and autologous fat was similar. However, considering that HA is, by far, the most used filler in the world for aesthetic procedures,[4,5] this observation suggests that autologous fat is more often associated with vascular complications than HA. Regarding the recovery rate of vascular complications, both HA and autologous fat were significantly associated with a lower frequency of improvement, but the latter showed a stronger trend towards more severe outcomes. This result is consistent with that of previous reviews, which concluded that autologous fat is the filler material that most frequently causes permanent blindness.[12,17,46] In a previous review by Beleznay et al,[12] autologous fat was responsible for 47.9 percent of cases of unilateral permanent blindness, followed by HA (23.5%), collagen (8.2%), poly-L-lactic acid (3.1%), and calcium hydroxylapatite (2%). The increased risk of major vascular complications associated with autologous fat injections could be explained by its large particle size, enabling it to occlude relatively large vessels, such as the ophthalmic artery.[12,17]

Regarding safety, one of the advantages of HA is the availability of an effective rescue procedure (i.e., hyaluronidase injection into or around the occluded blood vessel).[45,47,48] This is one of the reasons why HA has been claimed as the safest substance indicated for tissue augmentation.[48,49] However, in our review, the number of cases in which hyaluronidase was administered accounted for only a quarter of all cases in which HA was used (10 vs. 40). Furthermore, although the reduced number of cases limited our statistical analysis, it is worth mentioning that only half of these cases resulted in the total recovery of the main outcome related to vascular occlusion. The low recovery rate despite the use of hyaluronidase could be partially explained by the excessive time gap between symptoms onset and hyaluronidase injection, ranging from 3 to 24 hours, with five over seven cases exceeding the four-hour threshold, below which significant differences are seen.[45] These observations suggest that the safer profile of HA compared with autologous fat might be better explained by the properties of the filler material rather than the availability of a rescue procedure. Due to the different physical properties of each substance, the injector's ability to inject the filler using the right pressure might become an overriding factor influencing the risk of vascular complications.[12,50] Rapid injections not only result in greater amounts of filler but also limit the capacity of the injector to identify and amend any vascular occlusion. Furthermore, various authors have proposed that, when exerting too much pressure on the plunger, even during the injection of small amounts of filler, arterial pressure can easily be overcome, with the filler reaching deeper arteries.[6,12] Of course, injection pressure and rate cannot be monitored

unless the professional performing the injection uses a motorized injector to deliver the filler; hence, this information could not be included in our analysis. Motorized injectors have been proposed as a means to reduce injection risks, as they provide a comfortable flow rate and allow physicians to keep their attention on the patient.[50,51]

Considering that shorter onset times are more likely to prompt early interventions, we expected time to symptom onset to influence the outcome. However, no significant differences were found between the times before and after one hour. The importance of the time gap between the vascular complication and the intervention was investigated in animal models by Kim et al[38] and Cavallini et al,[47] who found that rescue procedures performed less than four hours after a filler injection significantly reduced the area of necrotic ear skin. However, these studies were based on hyaluronidase injections as rescue procedures, which were barely used in our case collection. Notwithstanding the lack of correlation with other studies, two important drawbacks limited our analysis of the potential influence of the time-to-onset on symptom recovery. First, our dataset did not include time frames more accurate than a 24-hour interval. Second, most of these cases were reported by ophthalmologists with patients showing sudden blindness concurrent with filler injections; therefore, the time from the aesthetic intervention to the onset of vision loss or blindness was assessed retrospectively.

Our results also showed that the affected blood vessel significantly influenced the outcome of the vascular complication. Based on the statistical analysis, ophthalmic artery occlusion was more frequently associated with no improvement than that of other blood vessels, particularly the nasociliary artery. However, individual case examinations revealed that the most dangerous adverse events (i.e., cerebral infarctions) occurred as an ultimate consequence of retinal artery occlusion. Since the retinal artery is a final branch of the ophthalmic artery, it could be assumed that an occlusion of the retinal artery is not likely to have consequences at more central areas. However, as previously discussed, when the tip of the needle penetrates the artery and pressure is applied to the plunger, the filler can reverse the flow in it, moving as a column proximal to the origin of the retinal artery. If the injector exerts more pressure on the plunger for a longer time, the column can reach the origin

TABLE 4. Recommendations for preventing and managing vascular complications associated with filler injections

PREVENTIVE STRATEGIES
Practitioner
Deep knowledge of the vascular anatomy is key for preventing vascular complications. In addition to good anatomical background knowledge, practitioners should consider the following aspects: • Possible altered anatomical connections in patients with previous surgeries • Possible anatomical variants during the development of some blood vessels; precaution should be taken in all face areas, including the upper lip and the wing of the nose • Possible extended vascular anastomoses of the nasal region from the perioral to the periorbital region, which might spread the filler from one area to the other.
Filler choice
Use reabsorbable products appropriate for the type of correction and therefore for the implant level. Hyaluronic acid fillers are typically noninflammatory products and have a purely mechanical effect, unlike collagen and autologous fat, which seem to activate the "clotting mechanism."
Injection technique
• Use a delicate retrograde injection technique. • Use very slow injection rates. • Apply light pressure on the syringe plunger (consider the use of an electronic device). • Distribute the product in various points by injecting small amounts of it (i.e. <0.1 mL). • Use a microcannula for deep injections and very viscous products (strongly recommended). • Use fine needles only for superficial injections. • Always aspirate before injection.
MANAGEMENT OF COMPLICATIONS
Immediate pain and/or bleaching of the area (typically a few seconds after injection)
Immediately stop injecting; vigorously massage the area.
Possible livedoreticularis or reactive hyperemia (it may occur up to 10 minutes after injection)
Treat immediately to restore the vascular flow.
Possible arterial insufficiency (slow capillary reloading with acupressure)
Apply warm gauzes, topical paste or patch of nitro-derivatives; inject hyaluronidase (independently from the type of filler injected) and apply a local massage.
Dark-blue discoloration of the area (it may occur from ten minutes to hours)
Contact your plastic surgeon and consider using systemic antibiotics, steroids, aspirin, low molecular weight heparin, prostaglandin.
Blisters and boils after a few days
Gently disinfect by swabbing the area; pierce the boils and gently favor the spillage of the serum; leave a gras gauze dressing with antibiotic on the skin for no more than three days, then remove it (with clamp and scissors), gently disinfect with 3% boric acid and medicate with a gras gauze dressing and antibiotic ointment until complete repitelization of the area.
Necrosis (can appear after days or weeks)
Apply antibiotic ointments until eschar demarcation; after removal of the necrotic tissue, apply products intended to improve tissue regeneration such as hydrocolloids gel, plates or collagen tablets on the loss of residual substance.
Ocular complications
Contact an eye surgeon immediately. In the meantime, try to reduce eye pressure through ocular massage, timolol drops, acetazolamide/manitol, steroids, haemodilution, oxygen therapy, antiplatelet/anticoagulant, thrombolysis, decompression of the eye anterior chamber.

of the ophthalmic artery, and part of the filler embolus can access the internal carotid artery and subsequently reach cerebral circulation (Figure 2).[6,12] The use of motorized devices, which enable accurate pressure control, has been proposed to minimize this risk.[50,51] We found no differences in the outcome when the occlusion occurred in other blood vessels, particularly the nasociliary and facial arteries. Although this observation is consistent with the larger diameter of these vessels, due to the limited number of cases in which there was occlusion in blood vessels other than the ophthalmic and retinal arteries, no firm conclusions could be reached.

Finally, we addressed the influence of the injection site on the outcome of the vascular event. Previous studies reported the glabella and the forehead as areas more frequently associated with blindness and visual loss than the nose.[5,7,11] However, in our analysis, injections in the nose accounted for nearly half of the cases of vascular complications and had a similar frequency to that of injections in the glabella. These observations indicated that the nose might not be a safer injection site than the glabella. Lazzeri et al[11] suggested that the dorsal nasal artery (i.e., the second terminal branch of the ophthalmic artery) might be responsible for the transmission of emboli following injections in either the glabella or the area proximal to the nasal root. Other injection sites did not yield significant results upon comparing the outcomes of the vascular procedures. However, it is worth mentioning that our analysis was compromised by the fact that a single patient could be injected at various sites, which precludes the identification of the precise injection responsible for the vascular complication.

Limitations. The fact that our meta-analysis was based mostly on case reports implies some limitations that should not be dismissed. Case reports do not always provide all details of the procedures performed. This was particularly notable for some variables identified as risk factors for vascular complications, such as injection technique, injected volume, pressure applied, and needle diameter, which were omitted in most cases. Some of these factors were investigated by Glogau et al,[5] who concluded that low injection pressures (i.e., flow rates of less than 0.3mL/minute) and small volume injections (i.e., less than 0.5mL) might prevent retrograde embolization of the filler; the authors also recommended avoiding the fan-like technique, which was identified as the main cause of iatrogenic vascular occlusion. Other variables that could not be analyzed because of data omission, despite their potential interest, include the specialty of the person performing the injection, the characteristics of the device (e.g., needle, cannula), and the concentration of hyaluronidase used in the rescue procedure. In addition to a few poor-quality case reports, some of the cases analyzed were not reported by the physician injecting the filler but rather by the ophthalmologist who treated the complication, thus omitting details of the initial aesthetic procedure. The variables most affected by this lack of data were time-to-onset, initial rescue treatment, and concomitant symptoms, which, in most cases, were retrospectively reported by the physician treating the complication. Another potential source of inaccuracy was the ad-hoc data transformation. The heterogeneity in the way the various case reports reported the data prevented the use of pure, raw data for the analysis, which would have been a factor adding simplicity and clarity to our conclusion.

In addition to presenting an updated and quantitative perspective of vascular complications associated with filler injections, the results obtained in our analysis might serve to support a few recommendations to help clinicians who perform filler augmentation procedures avoid vascular adverse events or minimize their consequences. Table 4 provides a list of key recommendations for preventing and minimizing vascular adverse events when performing filler injections. However, as mentioned before, our analysis has important limitations associated with the accuracy and diversity of data presentation in the source articles. Hence, the recommendations we present in Table 4 should not be interpreted as being strictly supported by the results of our meta-analysis; our recommendations are also based on our own insights gained from our extensive experience as plastic surgeons.

CONCLUSION

This meta-analysis provides an up-to-date overview of vascular complications associated with the injection of facial fillers. Our results support the hypothesis that autologous fat is more likely to cause serious vascular events than HA, irrespective of the use of hyaluronidase to treat the vascular occlusion. In light of the information published in the literature, it seems that accidental injection in the terminal branches of the facial artery, particularly the retinal artery, almost invariably leads to unilateral, and occasionally bilateral, blindness. The incidental occlusion of the retinal artery most frequently occurs when treating the nose, but this artery can also be reached from the glabella. Thus, to prevent vascular adverse effects, it is essential that the physician performing the filler injections has a proficient knowledge of anatomy.

ACKNOWLEDGMENTS

The authors gratefully acknowledge the time and effort of Dr. Patrice Delobel, Dr. Kévin Legent, and Dr. Luana Consolini, who provided scientific advice and helped with laying the groundwork of this research. The authors also thank the i2e3 Biomedical Research Institute team for providing statistical and medical writing assistance.

REFERENCES

1. Funt D, Pavicic T. Dermal fillers in aesthetics: an overview of adverse events and treatment approaches. *Clin Cosmet Investig Dermatol.* 2013;6(1):295–316.
2. Grunebaum LD, Allemann IB, Dayan S, et al. The risk of alar necrosis associated with dermal filler injection. *Dermatologic Surg.* 2009;35(Suppl 2):1635–1640.
3. Bailey SH, Cohen JL, Kenkel JM. Etiology, prevention, and treatment of dermal filler complications. *Aesthet Surg J.* 2011;31(1):110–121.
4. Matarasso SL, Carruthers JD, Jewell ML. Consensus recommendations for soft-tissue augmentation with nonanimal stabilized hyaluronic acid (Restylane). *Plast Reconstr Surg.* 2006;117(Suppl 3):3S–34S; discussion 35S–43S.
5. Glogau RG, Kane MAC. Effect of injection techniques on the rate of local adverse events in patients implanted with nonanimal hyaluronic acid gel dermal fillers. *Dermatologic Surg.* 2008;34(Suppl 1):S105–S109.
6. Carruthers A, Carruthers J. Non-animal-based hyaluronic acid fillers: scientific and technical considerations. *Plast Reconstr Surg.* 2007;120(6):33S–40S.
7. Weinberg MJ, Solish N. Complications of hyaluronic acid fillers. *Facial Plast Surg.* 2009;25(5):324–328.
8. Bachmann F, Erdmann R, Hartmann V, et al. The spectrum of adverse reactions after treatment with injectable fillers in the glabellar region: results from the injectable filler safety study. *Dermatologic Surg.* 2009;35(Suppl 2):1629–1634.
9. McCracken MS, Khan JA, Wulc AE, et al. Hyaluronic acid gel (Restylane) filler for facial rhytids: lessons learned from American Society of Ophthalmic Plastic

and Reconstructive Surgery member treatment of 286 patients. *Ophthal Plast Reconstr Surg.* 2006;22(3):188–191.
10. Zielke H, Wölber L, Wiest L, Rzany B. Risk profiles of different injectable fillers: results from the Injectable Filler Safety Study (IFS Study). *Dermatologic Surg.* 2008;34(3):326–335.
11. Lazzeri D, Agostini T, Figus M, et al. Blindness following cosmetic injections of the face. *Plast Reconstr Surg.* 2012;129(4):995–1012.
12. Beleznay K, Carruthers JDA, Humphrey S, Jones D. Avoiding and treating blindness from fillers: a review of the world literature. *Dermatologic Surg.* 2015;41(10):1097–1117.
13. Chen YY, Wang WY, Li JP, et al. Fundus artery occlusion caused by cosmetic facial injections. *Chin Med J (Engl).* 2014;127(8):1434–1437.
14. Loh KTD, Chua JJ, Lee HM, et al. Prevention and management of vision loss relating to facial filler injections. *Singapore Med J.* 2016;57(8):438–443.
15. Walker L, King M. This month's guideline: visual loss secondary to cosmetic filler injection. *J Clin Aesthet Dermatol.* 2018;11(5):E53–E55.
16. Urdiales-Gálvez F, Delgado NE, Figueiredo V, Lajo-Plaza J V, et al. Treatment of soft tissue filler complications: expert consensus recommendations. *Aesthetic Plast Surg.* 2018;42(2):498–510.
17. Feinendegen DL, Baumgartner RW, Vuadens P, et al. Autologous fat injection for soft tissue augmentation in the face: a safe procedure?. *Aesthetic Plast Surg.* 1998;22(3):163–167.
18. Park KH, Kim YK, Woo SJ, et al. Iatrogenic occlusion of the ophthalmic artery after cosmetic facial filler injections: a national survey by the Korean Retina Society. *JAMA Ophthalmol.* 2014;132(6):714–723.
19. Beasley TM, Schumacker RE. Multiple regression approach to analyzing contingency tables: post hoc and planned comparison procedures. *J Exp Educ.* 1995;64(1):79–93.
20. Kim SK, Kim JH, Hwang K. Skin necrosis of the nose after injection of ribose cross-linked porcine atelocollagen. *J Craniofac Surg.* 2015;26(7): 2211–2212.
21. Chou CC, Chen HH, Tsai YY, et al. Choroid vascular occlusion and ischemic optic neuropathy after facial calcium hydroxyapatite injection—a case report. *BMC Surg.* 2015;15(1):21.
22. Lin YC, Chen WC, Liao WC, Hsia TC. Central retinal artery occlusion and brain infarctions after nasal filler injection. *QJM.* 2015;108(9):731–732.
23. McGuire LK, Hale EK, Godwin LS. Post-filler vascular occlusion: a cautionary tale and emphasis for early intervention. *J Drugs Dermatol.* 2013;12(10): 1181–1183.
24. Kim EG, Eom TK, Kang SJ. Severe visual loss and cerebral infarction after injection of hyaluronic acid gel. *J Craniofac Surg.* 2014;25(2):684–686.
25. Hu XZ, Hu JY, Wu PS, et al. Posterior ciliary artery occlusion caused by hyaluronic acid injections into the forehead: a case report. *Medicine (Baltimore).* 2016;95(11):e3124.
26. Sung MS, Kim HG, Woo KI, Kim YD. Ocular ischemia and ischemic oculomotor nerve palsy after vascular embolization of injectable calcium hydroxylapatite filler. *Ophthal Plast Reconstr Surg.* 2010;26(4): 289–291.
27. Kim DY, Eom JS, Kim JY. Temporary blindness after an anterior chamber cosmetic filler injection. *Aesthetic Plast Surg.* 2015;39(3):428–430.
28. Roberts SAI, Arthurs BP. Severe visual loss and orbital infarction following periorbital aesthetic poly-(L)-lactic acid (PLLA) injection. *Ophthal Plast Reconstr Surg.* 2012;28(3):e68–e70.
29. Kim YJ, Choi KS. Bilateral blindness after filler injection. *Plast Reconstr Surg.* 2013;131:298e–299e.
30. Kwon SG, Hong JW, Roh TS, et al. Ischemic oculomotor nerve palsy and skin necrosis caused by vascular embolization after hyaluronic acid filler injection: a case report. *Ann Plast Surg.* 2013;71(4):333–334.
31. Kim SN, Byun DS, Park JH, et al. Panophthalmoplegia and vision loss after cosmetic nasal dorsum injection. *J Clin Neurosci.* 2014;21(4):678–680.
32. Kassir R, Kolluru A, Kassir M. Extensive necrosis after injection of hyaluronic acid filler: case report and review of the literature. *J Cosmet Dermatol.* 2011;10(3):224–231.
33. Carle M V, Roe R, Novack R, Boyer DS. Cosmetic facial fillers and severe vision loss. *JAMA Ophthalmol.* 2014;132(5):637–639.
34. Kim SG, Lee CJ, Kim YJ, Lee S Il. Salvage of nasal skin in a case of venous compromise after hyaluronic acid filler injection using prostaglandin E. *Dermatol Surg.* 2011;37(12):1817–1819.
35. Lee CM, Hong IH, Park SP. Ophthalmic artery obstruction and cerebral infarction following periocular injection of autologous fat. *Korean J Ophthalmol.* 2011;25(5):358.
36. Park SH, Sun HJ, Choi KS. Sudden unilateral visual loss after autologous fat injection into the glabellar area. *Clin Ophthalmol.* 2008;2(3):679–683.
37. Kwon DY, Park MH, Koh SB, et al. Multiple arterial embolism after illicit intranasal injection of collagenous material. *Dermatologic Surg.* 2010;36(7):1196–1199.
38. Kim YJ, Kim SS, Song WK, et al. Ocular ischemia with hypotony after injection of hyaluronic acid gel. *Ophthal Plast Reconstr Surg.* 2011;27(6):E152–E155.
39. Tracy L, Ridgway J, Nelson JS, et al. Calcium hydroxylapatite associated soft tissue necrosis: a case report and treatment guideline. *J Plast Reconstr Aesthetic Surg.* 2014;67(4):564–568.
40. Park SW, Woo SJ, Park KH, et al. Iatrogenic retinal artery occlusion caused by cosmetic facial filler injections. *Am J Ophthalmol.* 2012;154(4):653–662.
41. Park TH, Seo SW, Kim JK, Chang CH. Clinical experience with Hyaluronic acid-filler complications. *J Plast Reconstr Aesthetic Surg.* 2011;64(7):892–897.
42. Kim YK, Jung C, Woo SJ, Park KH. Cerebral angiographic findings of cosmetic facial filler-related ophthalmic and retinal artery occlusion. *J Korean Med Sci.* 2015;30(12):1847–1855.
43. Hong JH, Ahn SJ, Woo SJ, et al. Central retinal artery occlusion with concomitant ipsilateral cerebral infarction after cosmetic facial injections. *J Neurol Sci.* 2014;346(1–2):310–314.
44. Lee SK, Kim SM, Cho SH, et al. Adverse reactions to injectable soft tissue fillers: memorable cases and their clinicopathological overview. *J Cosmet Laser Ther.* 2015;17(2):102–108.
45. Kim DW, Yoon ES, Ji YH, et al. Vascular complications of hyaluronic acid fillers and the role of hyaluronidase in management. *J Plast Reconstr Aesthetic Surg.* 2011;64(12):1590–1595.
46. Rzany B, DeLorenzi C. Understanding, avoiding, and managing severe filler complications. *Plast Reconstr Surg.* 2015;136(5S):196S–203S.
47. Cavallini M, Gazzola R, Metalla M, Vaienti L. The role of hyaluronidase in the treatment of complications from hyaluronic acid dermal fillers. *Aesthet Surg J.* 2013;33(8):1167–1174.
48. Buhren BA, Schrumpf H, Hoff NP, et al. Hyaluronidase: from clinical applications to molecular and cellular mechanisms. *Eur J Med Res.* 2016;21(1):5.
49. Vartanian AJ, Frankel AS, Rubin MG. Injected hyaluronidase reduces restylane-mediated cutaneous augmentation. *Arch Facial Plast Surg.* 2005;7(4): 231–237.
50. Carey W, Weinkle S. Retraction of the plunger on a syringe of hyaluronic acid before injection: are we safe?. *Dermatologic Surg.* 2015;41(c):S340–S346.
51. Cassuto D, Papagni M. Anteis injection system: positive results of a preliminary clinical evaluation. *Updat Plast Surg.* 2010;3:5–8. JCAD

Cosmetic Filler–Induced Vascular Occlusion: A Rising Threat Presenting to Emergency Departments

Danny J. Soares, MD*; Stephanie D. Hynes, NP-C; Christina H. Yi, MD; Sabrina Shah-Desai, MS, FRCS; Steven C. Irving, MD

*Corresponding Author. E-mail: drsoares@plasticsurgeryvip.com.

Vascular emergencies from cosmetic filler–induced vascular occlusion represent an iatrogenic etiology that poses a threat to patients, with sequelae that range from disfiguring skin necrosis to blindness and stroke. As cosmetic fillers continue to grow in popularity, the importance of early identification, triaging, and management of these rare but potentially disabling injuries has motivated efforts to educate the public and professional audiences. In this practice review article, we outline components of acute care pertaining to these injuries based on evolving practice guidelines and best evidence recommendations. [Ann Emerg Med. 2024;83:59-67.]

0196-0644/$-see front matter

https://doi.org/10.1016/j.annemergmed.2023.07.006

INTRODUCTION

Dermal fillers have changed the landscape of plastic surgery, emerging as one of the most popular cosmetic treatments of the 21st century.[1] Designed for ease of injection, this class of soft implants is formulated with a variety of biocompatible/resorbable gels approved for dermal and subcutaneous placement.[2] Given their versatility and affordability, these products have evolved beyond "wrinklefilling" and are now routinely employed in facial sculpting.[3,4] With the rise in demand, the incidence of filler-induced vascular occlusion has also grown, with complications ranging from facial skin necrosis to blindness and stroke. This notable uptick in adverse outcomes has prompted the US Food & Drug Administration (FDA) to relabel filler products and call for improved training in the early identification and treatment of these injuries.[5-8] Given the potential for patients with filler-induced vascular occlusion to present to emergency departments (EDs), ED professionals should be equipped with current knowledge on this time-sensitive condition. In this article, we offer guidelines based on current evidence and consensus guidelines, recognizing the need for cautious interpretation and implementation due to the still-limited quality of supporting evidence.

EPIDEMIOLOGY

Filler-induced vascular occlusion injuries are rare occurrences, estimated at 0.01 to 0.05% per treatment based on retrospective studies.[9-11] However, given the rapid rise in popularity of dermal fillers, with more than 4 million treatments performed in the United States alone in 2022, filler-induced vascular occlusion injuries have seen a corresponding increase in incidence.[1,12,13] These figures are likely to grow given the increasing number of nonspecialized practitioners performing these treatments and an alarming trend of patient self-injections.[14-17] In the last 2 decades, the medical literature has chronicled a 30-fold increase in the number of skin necrosis and tripling of blindness/stroke due to filler-induced vascular occlusion.[5,6] Despite this, the true incidence of these injuries remains unknown and is likely underestimated due to the voluntary nature of the Manufacturer and User Facility Device Experience system responsible for cataloging these occurrences. Between 2015 and 2020, Manufacturer and User Facility Device Experience accrued a total of 5,009 unspecified "serious" injuries, 470 specified vascular adverse events, and 92 instances of visual impairment resulting from dermal fillers, with two-thirds of patients with vision loss incurring permanent deficits.[8]

PATHOPHYSIOLOGY

Filler-induced vascular occlusion represents an impending tissue infarction caused by the accidental injection of dermal filler into an artery, resulting in blockage, distal embolization, thrombosis, and possible spasm of the affected arterial network.[18] This effect creates an injury akin to *embolia cutis medicamentosa* (also known as Nicolau syndrome), leading to tissue ischemia and irreversible damage.[19] Because the face is supplied by the internal and external carotid arterial systems, which feature communicating anastomoses, the potential ramifications of

filler-induced vascular occlusion include facial skin necrosis, vision loss, and stroke, among others (Table 1).[5] Given the limited ischemic tolerance of tissues, ranging from 1.5 to 4.5 hours for the retina/brain to approximately 24 hours for the skin, early recognition and treatment of this etiology is essential.[20-22] Consequently, the primary goal in the treatment of filler-induced vascular occlusion is the prompt restoration of tissue perfusion and oxygenation whenever possible.

FILLER AGENTS

Since the introduction of Restylane (Galderma Laboratories) into the US market in 2003, numerous fillers have gained FDA approval for cosmetic use. Hyaluronic acid gels, comprising approximately 80% of all products used in the United States, currently dominate the filler market due to their versatility and rapid reversibility via existing hyaluronidase solutions. Consequently, hyaluronic acid fillers also account for approximately 80% of all filler-induced vascular occlusion injuries.[6] The remaining products consist of nonreversible fillers, such as calcium hydroxylapatite, polymethylmethacrylate, poly-l-lactic acid, liquid silicone, and autologous/allogeneic fat injections, which cannot be enzymatically degraded by hyaluronidase. For an up-to-date list of fillers, their indications, and reversibility, readers should refer to FDA's online registry.[2]

ILLUSTRATIVE CASE PRESENTATION 1

A healthy 47-year-old woman presented to the ED with acute-onset facial pain and skin discoloration located over the central part of the forehead.[23] Two days prior, she had received hyaluronic acid filler injections into the glabella for correction of frown lines by a cosmetic practitioner. During treatment, she experienced immediate pain over the forehead radiating to the left eye, with blanching of the central forehead skin (Figure 1A). Over the ensuing 48 hours, her pain worsened significantly and the affected skin became progressively darker. The patient denied experiencing visual or neurologic symptoms. Physical examination revealed livedoid discoloration, hyperemia, and pustular changes in the forehead with delayed capillary refill (Figure 1B). The result of the remainder of the physical examination, including neuro-ophthalmologic assessment, was normal.

Table 1. List of possible sequelae arising from filler-induced vascular occlusion of facial origin.

Arterial*	Venous
Muco-cutaneous/soft-tissue necrosis	Local venous thrombophlebitis
Vision loss ± ophthalmoplegia	Cerebral sinus thrombosis
Ischemic cerebral stroke	Pulmonary embolism
Facial paralysis/peripheral nerve injury	Myocardial infarction (PFO)

PFO, patent foramen ovale.
*Arterial injuries may still arise from venous inoculations due to the presence of arteriovenous shunts.

Clinical Presentation—Filler-Induced Skin Ischemia

Facial skin ischemia is the most common injury resulting from filler-induced vascular occlusion, threatening disfiguring skin necrosis. Severe pain (77%) and skin discoloration (67%) are the most common presenting symptoms based on a recent systematic review of 247 cases.[6] However, variations in early presentation may occur, in which pain may be minimal due to the effect of topical/local anesthetics employed during treatment, and skin changes may be imperceptible due to bruising, darker skin type, or intraoral/nasal location of the injury. Nonetheless, as the condition progresses, the characteristic features of pain, tenderness, and superficial skin changes become increasingly prevalent.[24] Thus, the presence of severe pain incongruent with examination findings occurring in the setting of recent cosmetic filler injections should elicit a high degree of suspicion for filler-induced vascular occlusion.

In filler-induced vascular occlusion–associated skin ischemia, the appearance of the skin often progresses through a series of distinctive stages (Figure 2). Initially, within minutes, pallor, palpable coolness, and delayed capillary refill time become evident. These dermal changes reflect impaired arterial flow in the dermal/subdermal plexuses.[25] If the arterio-occlusive injury persists, *livedo racemosa,* a reticular purpuric discoloration of the skin (due to pooling of deoxygenated blood in the dermis), appears within hours.[26] Left untreated, dermal ischemia results in deteriorating skin barrier function, leading to overgrowth of skin flora, presenting as comedones/pustules over the ensuing 2 to 5 days. With further injury progression, the skin gradually necroses, producing an eschar over 7 to 14 days that eventually extrudes, leaving an atrophic scar.[6,18,24] Although the skin may tolerate approximately 24 hours of warm complete ischemia (and longer periods of cold or partial ischemia), once the process of necrosis is underway, tissue loss is irreversible.

ED Evaluation and Diagnosis

The diagnosis of filler-induced vascular occlusion–associated skin ischemia should initiate an immediate time-sensitive evaluation of the patient that includes a detailed description of the inciting treatment.

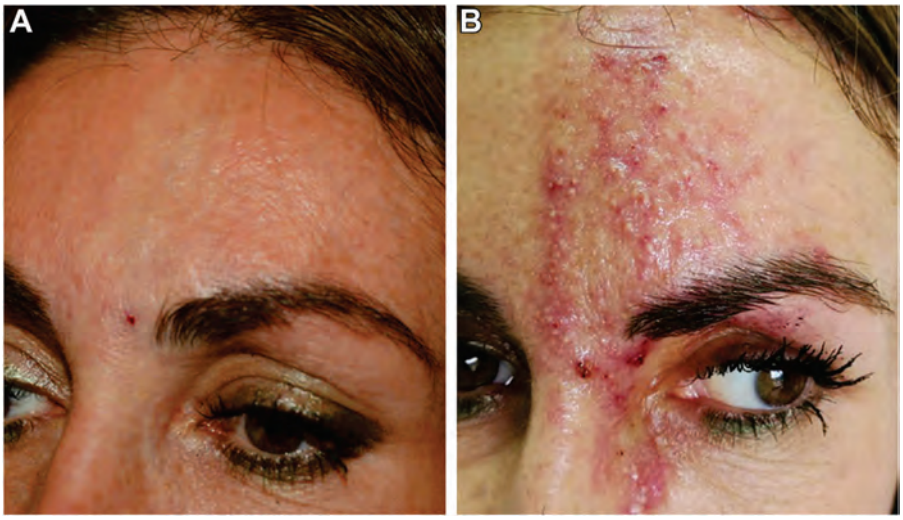


Figure 1. Patient from clinical scenario 1. *A,* Appearance immediately upon onset of injury, with pallor of the left central part of the forehead and superior nasal dorsum. *B,* Appearance 24 hours after injury showing livedoid skin discoloration with inflammatory pustular changes. (From Zambacos et al,[23] with permission.)

Information on the time of injection, area(s) treated, type of filler employed, and measures taken since injury should be elicited. The facial skin and mucosa should be inspected, observing for regions of pallor, delayed capillary refill time (>3 seconds), livedoid discoloration, or inflammatory/necrotic changes. The location and extent of the affected skin region depends on the arterial territory affected (eg, facial, ophthalmic, distal external carotid, and internal maxillary arteries), as illustrated in Figure E1 (available at http://www.annemergmed.com).[6] The affected territory, or angiosome, bears significance in terms of possible associated injuries and can help guide the examination. For instance, patients with skin ischemia involving the ophthalmic territory carry a nearly 50-fold greater risk of vision loss and 10-fold greater risk of stroke compared with those in patients with nonophthalmic skin injuries.[6] Furthermore, injuries affecting the ophthalmic or internal maxillary artery territories are more likely to harbor occult oral/nasal mucosal injuries (Figure 3).[27] A neuro-ophthalmologic examination should be conducted in all cases, along with an assessment of the oral and nasal cavities. The differential diagnosis of filler-induced vascular occlusion–associated skin ischemia is listed in Table 2 and includes a variety of potential etiologies associated with skin discoloration and arterial failure. Infectious and allergic etiologies can be excluded on the basis of clinical history and absence of ischemic skin signs. A recent history of facial filler injections occurring within days of presentation should alert the practitioner to the possibility of filler-induced vascular occlusion.

Management of Filler-Induced Skin Ischemia

Successful management of filler-induced skin ischemia is dependent on the early recognition and prompt reversal of the vascular occlusion. A treatment algorithm with therapeutic options to consider is displayed in Figure 4.

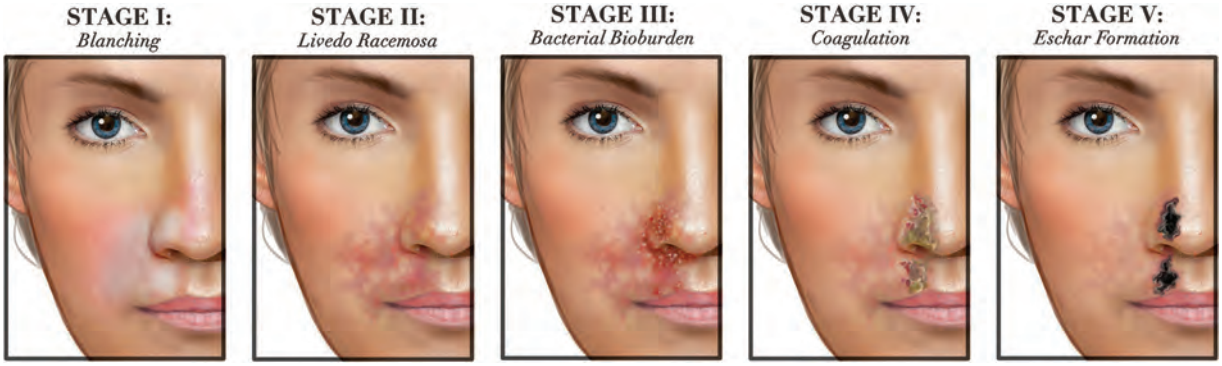


Figure 2. Clinical stages of ischemic skin injury. (From Soares et al,[6] with permission.)

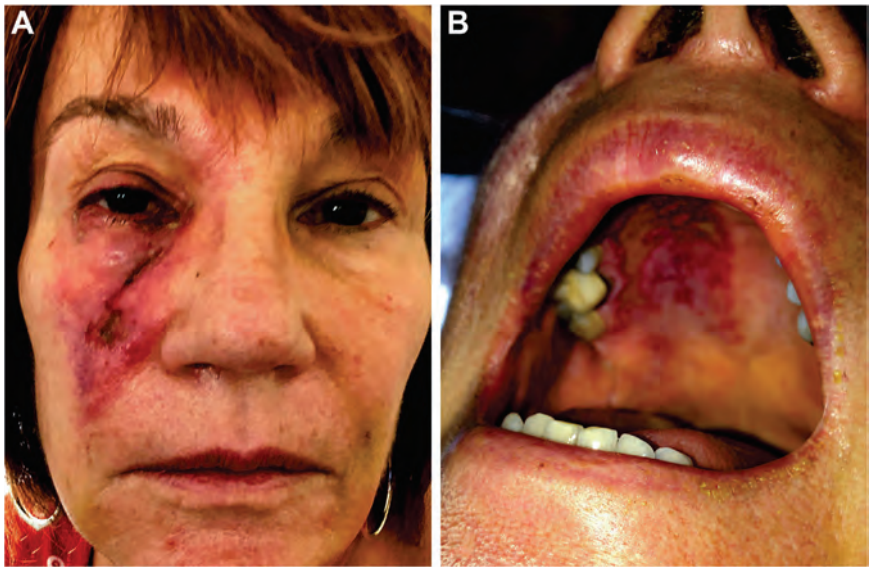


Figure 3. Example of a patient with filler-induced vascular occlusion arising from accidental injection of calcium hydroxylapatite filler into the right infraorbital artery. *A*, The external injury consisted of livedoid skin changes characteristic of early ischemia. *B,* The hemipalatal mucosal injury resulting from retrograde flow within the distal internal maxillary artery, leading to occlusion of the palatine arterial supply, was initially missed by the patient's treating provider. (From Soares et al,[27] with permission.)

Upon diagnosis, oral antiplatelet therapy with aspirin 325 mg (or clopidogrel 300mg if aspirin sensitive) is recommended based on extrapolation from other arterio-occlusive conditions, such as acute coronary and Nicolau syndromes, although studies specific to filler-induced vascular occlusion are lacking.[28-30] Warm compresses and soft-tissue massaging are advocated as a rapid means of improving tissue perfusion through local vasodilation and mechanical pumping, respectively.[31,32] Topical vasodilators (eg, nitroglycerin paste), traditionally employed in filler-induced vascular occlusion due to known benefits to ischemic postsurgical tissues, may be considered, although studies in humans are lacking and animal studies have shown a propensity toward venous congestion.[33,34] Systemic vasodilators (eg, oral phosphodiesterase-5 inhibitors) are not currently advocated due to lack of supporting evidence and the possibility of lowering tissue perfusion pressure.[35] Intravenous steroids should be considered in instances where severe edema and inflammation may be functionally impairing (eg, orbital/periorbital tissues), although their impact on tissue survival in filler-induced vascular occlusion has not been studied.[36,37]

Currently, reversal therapy with hyaluronidase remains the mainstay of treatment for filler-induced skin ischemia, offering a vital rescue pathway in cases involving hyaluronic acid fillers. In the United States, multiple hyaluronidase brands are available (Table E1, available at http://www.annemergmed.com), including human recombinant and animal-derived formulations. Consensus guidelines have been issued on the use of this reversal agent, but no human dosing studies specific to filler-induced vascular occlusion have been performed.[24,28-30] Hyaluronidase should be

Table 2. Differential diagnosis of filler-induced vascular occlusion skin injury.

Etiological Mechanism	Differential Diagnosis
Embolic	Nicolau syndrome Cholesterol crystal embolization Cryoglobulinemia Procedural (vascular embolization, sclerotherapy) Disseminated intravascular coagulation Septic embolism Calciphylaxis
Infectious	Bacterial cellulitis Necrotizing fasciitis Purpura fulminans (eg, disseminated meningococcemia) Viral (eg, *Zoster*)
Drug reaction	Warfarin necrosis Propylthiouracil-induced skin necrosis Acute and delayed hypersensitivity reaction
Inflammatory	Temporal arteritis Takayasu arteritis Cutaneous polyarteritis nodosa Antiphospholipid syndrome Livedoid vasculitis Sneddon syndrome

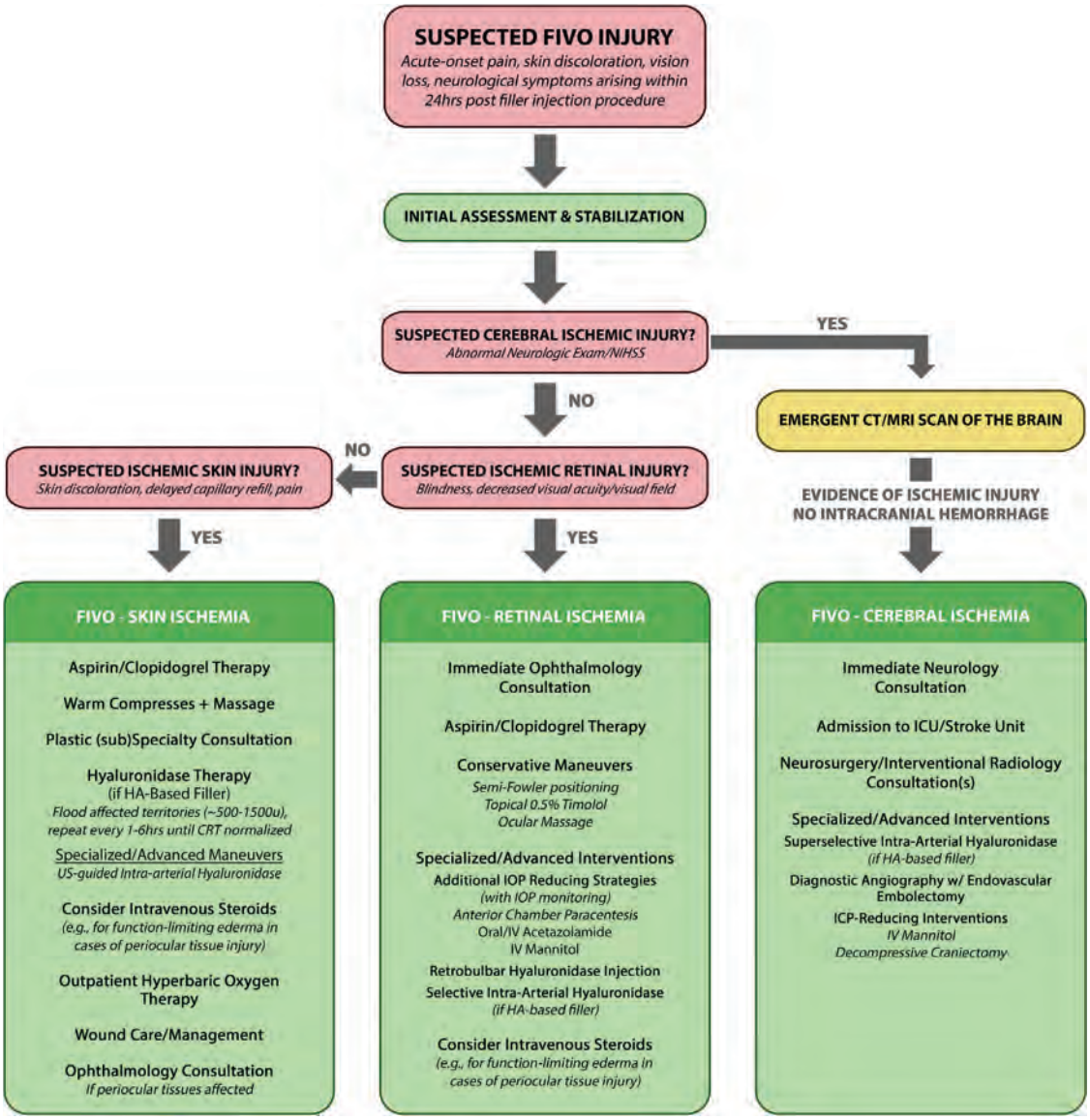


Figure 4. Proposed algorithm for the diagnostic and therapeutic approach to filler-induced vascular occlusion–associated injuries with treatment options to consider. *CRT*, capillary refill time; *CT*, computed tomography; *FIVO*, filler-induced vascular occlusion; *HA*, hyaluronic acid; *ICP*, intracranial pressure; *ICU*, intensive care unit; *IOP*, intraocular pressure; *IV*, intravenous; *MRI*, magnetic resonance imaging; *NIHSS*, National Institutes of Health stroke scale; *US*, ultrasound.

administered as soon as possible (preferably within the first 4 hours) at high doses (500 to 1500 U), with periodic readministration at least every 4 to 6 hours until clinical examination findings suggest return of perfusion (ie, normalization of capillary refill time and skin appearance).[31] The solution should be infiltrated via injection over the entire affected skin territory, aiming superficially (intradermal/subdermal) and deeply (subcutaneously) to target the skin's arterial supply. Given its safety and ease of use, hyaluronidase therapy can be administered by most practitioners, including emergency physicians, plastic surgeons, and other specialists (eg, dermatology, otolaryngology, ophthalmology, and oromaxillofacial surgery). Ultrasound guidance/mapping may help improve treatment precision by identifying regions of underperfusion, reducing the need for indiscriminate tissue flooding, and lowering the dose of hyaluronidase.[38]

In contrast, non–hyaluronic acid fillers are not amenable to hyaluronidase therapy, although in the absence of product information, attempted reversal is still recommended. Instances arising from nonreversible fillers benefit from an emphasis on modalities designed to enhance tissue oxygenation, such as hyperbaric oxygen

therapy, which has demonstrated benefit in multiple filler-induced vascular occlusion case series and therapeutic benefit in ischemic surgical wounds, flaps, and grafts.[39-42] When employed, hyperbaric oxygen therapy is typically initiated in the outpatient setting, ideally within 48 hours, following an accelerated regimen with once or twice daily treatment sessions over 1 week.[43]

Dispositionally, patients with isolated low-grade filler-induced vascular occlusion skin injuries may be managed in the outpatient setting after evaluation, stabilization, and initial reversal therapy in the ED with appropriate specialized outpatient follow-up. Repeated hyaluronidase treatments are often necessary for complete clearance of reversible (hyaluronic acid) filler occlusions in the first 48 hours, and close follow-up is advised to monitor for reocclusion from distal embolization of intra-arterial filler remnants.[31,44] For delayed presentations beyond 72 hours, in which tissue necrosis has already manifested, hyaluronidase injections should still be considered, and outpatient wound care management and hyperbaric oxygen therapy should be instituted to minimize scarring.[45] The patient presented in this study underwent immediate treatment with oral aspirin, hyaluronidase injections to the glabella, and topical nitroglycerine, followed by wound care with occlusive dressings; she ultimately healed favorably with mild scarring.

ILLUSTRATIVE CASE PRESENTATION 2

A 59-year-old woman presented to the ED with acute vision loss after hyaluronic acid filler treatment of frown lines 3 hours prior to arrival. Upon injection, she recalled experiencing sudden dizziness, nausea, and right frontal headache, followed by complete vision loss in the right eye. She received immediate hyaluronidase injections into the glabella and central forehead by her cosmetic provider, with little improvement. At the ED, evaluation revealed livedoid discoloration of the right supratrochlear region of the forehead (Figure 5A).[46] On ophthalmic examination, there was absence of light perception and an afferent pupillary defect in the right eye; visual acuity was normal in the left eye. Fundoscopic examination revealed a pale retina with occlusion of retinal vessels in the right eye and a normal retina in the left eye (Figure 5B and C); neurologic examination findings were normal. The patient received 650 mg of oral aspirin and warm compresses and topical nitroglycerin paste to the forehead. Plastic surgery and ophthalmology services were consulted, and human recombinant hyaluronidase was immediately administered into the orbit (1100 U via retrobulbar injection) and forehead skin (250 U). A magnetic resonance imaging scan of the brain revealed multiple punctate infarcts in the right frontal and occipital lobes.

Clinical Presentation—Filler-Induced Retinocerebral Ischemia

Retinal and cerebral ischemic injuries represent the most devastating instances of filler-induced vascular occlusion, threatening permanent visual and neurologic disability.[5,47] The mechanism of retinal and cerebral ischemic injuries is thought to involve the retrograde flow of a filler embolus toward the proximal ophthalmic and internal carotid arterial systems.[25] Because the retina is perfused solely by the central retinal artery, irreversible damage may occur

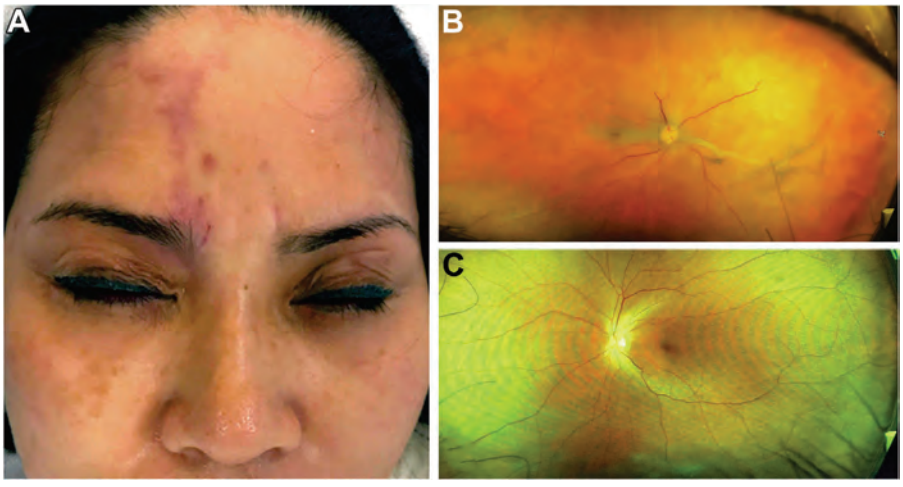


Figure 5. Patient from clinical scenario 2. *A*, The appearance of the patient upon presentation within 24 hours of injury. The right supratrochlear cutaneous segment of the forehead displays the characteristic livedoid skin discoloration typical of early ischemic injury. *B*, Ultra-widefield pseudocolor fundus image of the right eye showing a pale retina with attenuation of the retinal vessels. *C*, Ultra-widefield pseudocolor fundus image showing normal findings in the left eye. (From Moore et al,[46] with permission.)

after 30 to 90 minutes of ischemia.[20] In addition, cerebral ischemic injury is present in approximately 20% of filler-induced vascular occlusion instances of retinal infarction, with a therapeutic window of 3 to 4.5 hours.[5,22]

ED Evaluation and Diagnosis

The initial presentation of patients with filler-induced retinal and/or cerebral ischemia is often more severe and alarming due to functional deficits. On arrival, patients should undergo rapid screening via non-contrast computed tomography imaging in accordance with established stroke protocols. Given the ischemic nature of both filler-induced and atherosclerotic strokes, early differentiation between the 2 may be difficult and requires a targeted history with specific inquiry regarding recent cosmetic treatments. The onset of symptoms shortly after cosmetic filler injections, especially in a patient at low risk for atherosclerotic or cardioembolic cerebral stroke, should alert the physician to the rare possibility of filler-induced injury.

On examination, patients with orbital ischemia may demonstrate orbital edema/proptosis, skin discoloration (44%), blepharoptosis (52%), ophthalmoplegia (54%), and visual dysfunction ranging from mildly decreased acuity to complete loss of vision.[48] A grading scale of severity for periocular ischemic injuries has been proposed (Table E2).[49] Neurologic symptomatology, when present, typically relates to middle (67%) and anterior (26%) cerebral artery ischemia and includes altered consciousness, hemiplegia, facial paralysis, and abnormal speech.[5] Because most of these occurrences arise from filler injections into the ophthalmic angiosome (ie, the upper face), patients often show evidence of skin ischemia over the forehead and nose.[6] Dilated fundoscopic examination and/or fluorescein angiography may show evidence of arterial occlusion with retinal whitening, cherry red spot, or even visible filler emboli.[50] In the absence of overt neurologic symptoms, computed tomography and/or magnetic resonance imaging is still indicated in patients with retinal ischemia to screen for cerebral infarction, which may initially be asymptomatic.[6] Angiography may be helpful in better quantifying the extent of the perfusion defect.[51,44]

Management of Filler-Induced Retinocerebral Ischemia

The management of filler-induced retinal and cerebral ischemic injuries centers on the rapid delivery of specialized neuro-ophthalmologic care; however, therapeutic success still remains limited. Contributing factors to these modest rates of functional recovery may include therapeutic delays, and the type of filler material may also influence outcomes.[5,52-54] Specifically, injuries arising from reversible fillers (hyaluronic acid) have a more favorable outcome than that from non–hyaluronic acid injuries (32% versus 12% rate of visual recovery).[36,51] In addition, collateral blood supply via the cilioretinal artery, an arterial branch present in approximately 20% of retinas, favors a higher rate of partial visual recovery.[55,56]

Early conservative interventions, such as intraocular pressure–reducing measures (topical timolol 0.5% and semi-Fowler positioning), ocular massage, oxygen supplementation, and antiplatelet therapy, may be initiated before arrival or while awaiting further specialized care. In addition, other intraocular pressure/intracranial pressure–reducing interventions (oral acetazolamide, intravenous mannitol, carbogen/CO_2 rebreathing, and anterior chamber paracentesis) should be considered with appropriate intraocular pressure monitoring to enhance retinal blood flow, favoring no more than a 30% intraocular pressure reduction from baseline at presentation.[36] Systemic steroids, typically advocated for retinal ischemia of inflammatory etiology (eg, temporal arteritis), have not been studied in cases of filler-induced blindness, although they may be considered in expert consultation.[57,58,36]

Hyaluronidase therapy, although highly efficacious in hyaluronic acid–induced skin injuries, has shown minimal benefit in instances of retinal and cerebral ischemic injuries due difficulties in achieving rapid delivery of the enzyme into the orbital and cerebral vasculature.[47] Retrobulbar hyaluronidase therapy, in which hyaluronidase is administered via a 25-guage, 1.5-inch needle into the posterior orbit, requires expertise and has a high (>80%) rate of failure.[59-62] As a result, endovascular reperfusion therapy via selective intra-arterial hyaluronidase performed by interventional radiology has recently gained some support, achieving partial visual recovery in 42% of patients when combined with intra-arterial fibrinolytic therapy.[44] Nonetheless, the intrinsic risk of ischemic and hemorrhagic stroke with this approach and the significant capabilities and expertise required, in light of its incomplete efficacy, have limited its adoption beyond select tertiary centers.[63] For instances of hyaluronic acid filler–induced stroke, the effectiveness of endovascular hyaluronidase has not been evaluated.

The management approach and therapeutic success rates for ischemic cerebral injuries mirror those of retinal injuries, although additional invasive interventions, such as embolectomy, may be considered in the relevant setting.[5] Systemic anticoagulation and fibrinolytic therapy have not been recommended in cases of filler-induced stroke and blindness due to the associated risk of intracerebral hemorrhage and the nonthrombotic nature of the primary etiology.[5] Hyperbaric oxygen, although theoretically capable of prolonging tissue survival time, has not been

studied in cases of filler-induced vascular occlusion–associated retinal and cerebral ischemia.[64] Additional studies on the impact of hyperbaric oxygen as well as novel therapies, such as intravenous hyaluronidase, have been proposed and are currently needed.[65,66] In this case scenario, the patient did not recover visual function in the right eye and suffered minor skin necrosis with permanent scarring of the central region of the forehead.

In conclusion, filler-induced vascular injuries pose an increasingly frequent, although rare, threat with potentially devastating cosmetic and neuro-ophthalmologic sequelae. Rapid reversal therapy, when instituted promptly in select cases, can achieve high rates of therapeutic success in facial skin injuries. In contrast, filler-induced retinal and cerebral ischemia currently present a significant clinical challenge with traditionally poor outcomes. Practitioners should be aware of the signs and symptoms of these rare injuries and be ready to promptly implement treatment to improve the odds of therapeutic success whenever possible.

Supervising editor: Robert D. Welch, MD, MS. Specific detailed information about possible conflicts of interest for individual editors is available at https://www.annemergmed.com/editors.

Author affiliations: From the University of Central Florida (Soares), College of Medicine, Orlando, FL; American Foundation for Aesthetic Medicine (Soares, Hynes, Yi), Fruitland Park, FL; Ophthalmology/Oculoplastic Surgery (Shah-Desai), Private Practice, London, United Kingdom; and Department of Emergency Medicine (Irving), AdventHealth Hospital, Orlando, FL.

All authors attest to meeting the four ICMJE.org authorship criteria:(1) Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND (2) Drafting the work or revising it critically for important intellectual content; AND (3) Final approval of the version to be published; AND (4) Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Funding and support: By *Annals*' policy, all authors are required to disclose any and all commercial, financial, and other relationships in any way related to the subject of this article as per ICMJE conflict of interest guidelines (see www.icmje.org). The authors have stated that no such relationships exist. The authors report this article did not receive any outside funding or support.

Publication dates: Received for publication February 6, 2023. Revisions received May 1, 2023, and July 4, 2023. Accepted for publication July 10, 2023.

REFERENCES

1. Plastic surgery statistics report 2020. American Society of Plastic Surgeons. Accessed March 17, 2023. https://www.plasticsurgery.org/documents/News/Statistics/2020/plastic-surgery-statistics-full-report-2020.pdf
2. Approved uses of dermal fillers. Food and Drug Administration. Accessed March 17, 2023. https://www.fda.gov/medical-devices/aesthetic-cosmetic-devices/dermal-fillers-soft-tissue-fillers
3. Wilson AJ, Taglienti AJ, Chang CS, et al. Current applications of facial volumization with fillers. *Plast Reconstr Surg*. 2016;137:872e-89e.
4. Ugarte A, Blevins LW, Wills-Kofford JC, et al. Dermal filler re-contouring of the aged jawline: a useful non-surgical modality in facial rejuvenation. *J Aesthet Nurs*. 2022;11:70-78.
5. Wang HC, Yu N, Wang X, et al. Cerebral embolism as a result of facial filler injections: a literature review. *Aesthet Surg J*. 2022;42:NP162-NP175.
6. Soares DJ, Bowhay A, Blevins LW, et al. Patterns of filler-induced facial skin ischemia: a systematic review of 243 cases and introduction of the FOEM scoring system and grading scale. *Plast Reconstr Surg*. 2023;151:592e-608e.
7. Jagdeo J, Hruza G. The Food and Drug Administration safety communication on unintentional injection of soft-tissue filler into facial blood vessels: important points and perspectives. *Dermatol Surg*. 2015;41:1372-1374.
8. FDA executive summary general issues panel meeting on dermal fillers. Food and Drug Administration. Accessed March 17, 2023. https://www.fda.gov/media/146870/download
9. Beleznay K, Humphrey S, Carruthers JD, et al. Vascular compromise from soft tissue augmentation: experience with 12 cases and recommendations for optimal outcomes. *J Clin Aesthet Dermatol*. 2014;7:37-43.
10. Beleznay K, Carruthers JD, Humphrey S, et al. Avoiding and treating blindness from fillers: a review of the world literature. *Dermatol Surg*. 2015;41:1097-1117.
11. Alam M, Kakar R, Dover JS, et al. Rates of vascular occlusion associated with using needles vs cannulas for filler injection. *JAMA Dermatol*. 2021;157:174-180.
12. Beleznay K, Carruthers JDA, Humphrey S, et al. Update on avoiding and treating blindness from fillers: a recent review of the world literature. *Aesthet Surg J*. 2019;39:662-674.
13. ISAPS international survey on aesthetic/cosmetic procedures. International Society of Aesthetic Plastic Surgery. Accessed March 17, 2023. https://www.isaps.org/media/vdpdanke/isaps-global-survey_2021.pdf
14. Wang JV, Albornoz CA, Goldbach H, et al. Experiences with medical spas and associated complications: a survey of aesthetic practitioners. *Dermatol Surg*. 2020;46:1543-1548.
15. 2022 medical spa state of the industry report. American Med Spa Association. Accessed March 17, 2023. https://americanmedspa.org/resources/med-spa-statistics
16. Valiga A, Albornoz CA, Chitsazzadeh V, et al. Medical spa facilities and nonphysician operators in aesthetics. *Clin Dermatol*. 2022;40:239-243.
17. Bowhay A, Soares DJ. Acute vascular compromise of the ophthalmic cutaneous angiosome after accidental self-injection of hyaluronic acid filler into the superficial temporal artery. *Dermatol Surg*. 2021;47:1527-1529.
18. Soares DJ. Bridging a century-old problem: the pathophysiology and molecular mechanisms of ha filler-induced vascular occlusion (FIVO)-implications for therapeutic interventions. *Molecules*. 2022;27:5398.
19. Chen Y, Zhang YL, Luo SK. Experimentally induced arterial embolism by hyaluronic acid injection: clinicopathologic observations and treatment. *Plast Reconstr Surg*. 2019;143:1088-1097.
20. Hayreh SS, Zimmerman MB, Kimura A, et al. Central retinal artery occlusion. Retinal survival time. *Exp Eye Res*. 2004;78:723-736.
21. Tobalem S, Schutz JS, Chronopoulos A. Central retinal artery occlusion—rethinking retinal survival time. *BMC Ophthalmol*. 2018;18:101.
22. Bluhmki E, Chamorro A, Dávalos A, et al. Stroke treatment with alteplase given 3.0-4.5 h after onset of acute ischaemic stroke (ECASS III): additional outcomes and subgroup analysis of a randomised controlled trial. *Lancet Neurol*. 2009;8:1095-1102.
23. Zambacos GJ, Hapsas DA, Mandrekas AD. Glabella impending skin necrosis: a case report. *Eur J Plast Surg*. 2019;42:193-196.

24. Murray G, Convery C, Walker L, et al. Guideline for the management of hyaluronic acid filler-induced vascular occlusion. *J Clin Aesthet Dermatol*. 2021;14:E61-E69.
25. Ashton MW, Taylor GI, Corlett RJ. The role of anastomotic vessels in controlling tissue viability and defining tissue necrosis with special reference to complications following injection of hyaluronic acid fillers. *Plast Reconstr Surg*. 2018;141:818e-30e.
26. Parsi K. Dermatological manifestations of venous disease: part II. *Aust New Zeal J Phlebol*. 2007;10:7-15.
27. Soares DJ, Blevins LW. Distal internal maxillary artery occlusion with palatal necrosis following cheek injection with calcium hydroxylapatite. *Plast Reconstr Surg Glob Open*. 2022;10:e4164.
28. Cohen JL, Biesman BS, Dayan SH, et al. Treatment of hyaluronic acid filler-induced impending necrosis with hyaluronidase: consensus recommendations. *Aesthet Surg J*. 2015;35:844-849.
29. Signorini M, Liew S, Sundaram H, et al. Global aesthetics consensus: avoidance and management of complications from hyaluronic acid fillers—evidence- and opinion-based review and consensus recommendations. *Plast Reconstr Surg*. 2016;137:961e-71e.
30. King M. This month's guideline: management of necrosis. *J Clin Aesthet Dermatol*. 2018;11:E53-E57.
31. DeLorenzi C. New high dose pulsed hyaluronidase protocol for hyaluronic acid filler vascular adverse events. *Aesthet Surg J*. 2017;37:814-825.
32. Sun Y, Jin M, Wang G, et al. Early warm compress treatment can promote recanalization of vascular embolisms and reduce tissue necrosis after polymethyl methacrylate injection. *Sci Rep*. 2023;13:1872.
33. Wang P, Gu L, Qin Z, et al. Efficacy and safety of topical nitroglycerin in the prevention of mastectomy flap necrosis: a systematic review and meta-analysis. *Sci Rep*. 2020;10:6753.
34. Hwang CJ, Morgan PV, Pimentel A, et al. Rethinking the role of nitroglycerin ointment in ischemic vascular filler complications: an animal model with ICG imaging. *Ophthalmic Plast Reconstr Surg*. 2016;32:118-122.
35. da Cruz NFS, Polizelli MU, Cezar LM, et al. Effects of phosphodiesterase type 5 inhibitors on choroid and ocular vasculature: a literature review. *Int J Retina Vitreous*. 2020;6:38.
36. Graue G, Ochoa Araujo DA, Plata Palazuelos C, et al. The M.A.STE.R.S algorithm for acute visual loss management after facial filler injection. *J Cosmet Dermatol*. 2020;19:2859-2866.
37. Hwang SH, Lee JH, Kim BG, et al. The efficacy of steroids for edema and ecchymosis after rhinoplasty: a meta-analysis. *Laryngoscope*. 2015;125:92-98.
38. Schelke LW, Velthuis PJ, Decates T, et al. Ultrasound-guided targeted vs regional flooding: a comparative study for improving the clinical outcome in soft tissue filler vascular adverse event management. *Aesthet Surg J*. 2023;43:86-96.
39. Darling MD, Peterson JD, Fabi SG. Impending necrosis after injection of hyaluronic acid and calcium hydroxylapatite fillers: report of 2 cases treated with hyperbaric oxygen therapy. *Dermatol Surg*. 2014;40:1049-1052.
40. Oley MH, Oley MC, Mawu FO, et al. Hyperbaric oxygen therapy in managing minimally invasive aesthetic procedure complications: a report of three cases. *Clin Cosmet Investig Dermatol*. 2022;15:63-68.
41. Kruize RGF, Teguh DN, van Hulst RA. Hyperbaric oxygen therapy in hyaluronic acid filler-induced dermal ischemia. *Dermatol Surg*. 2020;46:1755-1757.
42. Dauwe PB, Pulikkottil BJ, Lavery L, et al. Does hyperbaric oxygen therapy work in facilitating acute wound healing: a systematic review. *Plast Reconstr Surg*. 2014;133:208e-15e.
43. Henderson R, Reilly DA, Cooper JS. Hyperbaric oxygen for ischemia due to injection of cosmetic fillers: case report and issues. *Plast Reconstr Surg Glob Open*. 2018;6:e1618.
44. Zhang LX, Lai LY, Zhou GW, et al. Evaluation of intraarterial thrombolysis in treatment of cosmetic facial filler-related ophthalmic artery occlusion. *Plast Reconstr Surg*. 2020;145:42e-50e.
45. Farmer A, Murray G, Croasdell B, et al. Facial vascular events and tissue ischemia: a guide to understanding and optimizing wound care. *J Clin Aesthet Dermatol*. 2021;14(suppl 1):S39-S48.
46. Moore RM, Mueller MA, Hu AC, et al. Asymptomatic stroke after hyaluronic acid filler injection: case report and literature review. *Aesthet Surg J*. 2021;41:NP602-NP608.
47. Chatrath V, Banerjee PS, Goodman GJ, et al. Soft-tissue filler-associated blindness: a systematic review of case reports and case series. *Plast Reconstr Surg Glob Open*. 2019;7:e2173.
48. Walker L, Convery C, Davies E, et al. Consensus opinion for the management of soft tissue filler induced vision loss. *J Clin Aesthet Dermatol*. 2021;14:E84-E94.
49. Myung Y, Yim S, Jeong JH, et al. The classification and prognosis of periocular complications related to blindness following cosmetic filler injection. *Plast Reconstr Surg*. 2017;140:61-64.
50. Tran AQ, Lee WW. Vision loss and blindness following fillers. *J Dermatol Skin Sci*. 2021;3:1-4.
51. Kim YK, Jung C, Woo SJ, et al. Cerebral angiographic findings of cosmetic facial filler-related ophthalmic and retinal artery occlusion. *J Korean Med Sci*. 2015;30:1847-1855.
52. Wang J, Shen H, Liu T, et al. An efficacy and safety study of intra-arterial recanalization of occluded ophthalmic arteries in patients with monocular blindness caused by injection of hyaluronic acid in facial tissues. *Aesthetic Plast Surg*. 2021;45:1573-1578.
53. Ardila Jurado E, Sturm V, Brugger F, et al. Central retinal artery occlusion: current practice, awareness and prehospital delays in Switzerland. *Front Neurol*. 2022;13:888456.
54. Chiang C, Zhou S, Chen C, et al. Intravenous hyaluronidase with urokinase as treatment for rabbit retinal artery hyaluronic acid embolism. *Plast Reconstr Surg*. 2016;138:1221-1229.
55. Kim YH, Park KH, Woo SJ. Clinical manifestations and visual prognosis of cilioretinal artery sparing central retinal artery occlusion. *Korean J Ophthalmol*. 2020;34:27-34.
56. Dattilo M, Newman NJ, Biousse V. Acute retinal arterial ischemia. *Ann Eye Sci*. 2018;3:28.
57. Hayreh SS, Zimmerman MB. Non-arteritic anterior ischemic optic neuropathy: role of systemic corticosteroid therapy. *Graefes Arch Clin Exp Ophthalmol*. 2008;246:1029-1046.
58. Rebolleda G, Pérez-López M, Casas-Llera P, Contreras I, Muñoz-Negrete FJ. Visual and anatomical outcomes of non-arteritic anterior ischemic optic neuropathy with high-dose systemic corticosteroids. *Graefes Arch Clin Exp Ophthalmol*. 2013;251:255-260.
59. Navarro-Hernandez E, Pérez-López M. Effectiveness of retrobulbar hyaluronidase in the treatment of visual loss caused by periocular hyaluronic acid injection. A systematic review. *Arch Soc Esp Oftalmol (Engl Ed)*. 2022;97:521-538.
60. Hwang CJ, Perry JD. Effectiveness of retrobulbar hyaluronidase injection in an iatrogenic blindness rabbit model using hyaluronic acid filler injection. *Plast Reconstr Surg*. 2020;145:658e-60e.
61. Lee W, Oh W, Ko HS, et al. Effectiveness of retrobulbar hyaluronidase injection in an iatrogenic blindness rabbit model using hyaluronic acid filler injection. *Plast Reconstr Surg*. 2019;144:137-143.
62. Zhu GZ, Sun ZS, Liao WX, et al. Efficacy of retrobulbar hyaluronidase injection for vision loss resulting from hyaluronic acid filler embolization. *Aesthet Surg J*. 2017;38:12-22.
63. Zhang L, Luo Z, Li J, et al. Endovascular hyaluronidase application through superselective angiography to rescue blindness caused by hyaluronic acid injection. *Aesthet Surg J*. 2021;41:344-355.
64. Lopes AS, Basto R, Henriques S, et al. Hyperbaric oxygen therapy in retinal arterial occlusion: epidemiology, clinical approach, and visual outcomes. *Case Rep Ophthalmol Med*. 2019;2019:9765938.
65. Olson EA, Lentz K. Central retinal artery occlusion: a literature review and the rationale for hyperbaric oxygen therapy. *Mo Med*. 2016;113:53-57.
66. Mccann M. Intravenous hyaluronidase for visual loss secondary to filler injection: a novel therapeutic approach. *J Clin Aesthet Dermatol*. 2019;12:25-27.

ATTACHMENT D

Experiences With Medical Spas and Associated Complications: A Survey of Aesthetic Practitioners

Jordan V. Wang, MD, MBE, MBA,* Christian A. Albornoz, MD,* Hayley Goldbach, MD,† Natasha Mesinkovska, MD, PhD,† Thomas Rohrer, MD,‡ Christopher B. Zachary, MBBS, FRCP,† and Nazanin Saedi, MD*

BACKGROUND Medical spas have experienced a recent rise in popularity. However, rules and regulations vary nationwide. Given the number of complications attributable to medical spas, questions remain about currently regulatory practices and whether they are sufficient to protect patients from harm.

OBJECTIVE Our study investigated the current state of medical spas and their associated patient complications in the aesthetic field as well as the experiences and attitudes of practitioners.

MATERIALS AND METHODS A survey was distributed to current members of the American Society for Dermatologic Surgery.

RESULTS Of all cosmetic complications encountered in the past 2 years, the majority reported that the percentage of complications seen in their practice attributable to medical spas ranged from 61% to 100%. The most commonly cited complications from medical spas were burn, discoloration, and misplacement of product, whereas the most commonly cited treatments resulting in complications were fillers, intense pulsed light, and laser hair removal. For safety and outcomes, medical spas were rated as inferior to physician-based practices.

CONCLUSION Patient complications associated with medical spas are not uncommon. Overall, practitioners believe medical spas are endangering to patient safety, think that stricter rules and regulations are necessary, and request more support from the specialty medical societies.

The authors have indicated no significant interest with commercial supporters.

In a society which places a growing value on aesthetic beauty, the prevalence of noninvasive and minimally invasive cosmetic procedures has continued to rise. A recent member survey of the American Society for Dermatologic Surgery (ASDS) demonstrated that in 2018, over 3.7 million injectable procedures were performed.[1] Injection of filler products experienced a 78% increase from 2012. Laser, light, and energy-based treatments grew by 74%, and body sculpting procedures increased over 400% during this time period. The increasing popularity of aesthetic treatments has undoubtedly contributed to the trend of medical spas opening across the country.

These aesthetically focused facilities offer treatments similar to those historically performed in physician-based practices—often at discounted prices—but with varying standards of oversight and credentialing. Ironically, the efforts of states to improve access to primary health care by loosening the regulations for nonphysician providers have fostered an appetite for more lucrative aesthetic services in a spa environment. These state legislations have created an influx of nonphysician providers practicing aesthetic services with either no or partial supervision, despite vocal opposition from various specialty societies, such as the ASDS and American Academy of Dermatology.[2,3] Owing to a gross lack of uniform regulations between

*Department of Dermatology and Cutaneous Biology, Thomas Jefferson University, Philadelphia, Pennsylvania; †Department of Dermatology, University of California, Irvine, California; ‡SkinCare Physicians, Chestnut Hill, Massachusetts

ISSN: 1076-0512 • Dermatol Surg 2020;00:1–5 • DOI: 10.1097/DSS.0000000000002344

states, the roles and responsibilities of providers have become increasingly blurred, and the divide between aesthetic dermatology and cosmetology has narrowed. The detrimental consequences of this shift are clear and have already resulted in various adverse events for patients and consumers.

Tracking adverse events attributable to nonphysicians or nondermatology providers is difficult. Previous studies have examined complication rates, but this does not paint a complete picture. Although the literature has consistently demonstrated low complication rates with most procedures, these studies have traditionally focused on board-certified dermatologists or plastic surgeons as opposed to other providers who may possess more limited training or skillset.[4] These reports may therefore underrepresent the true rate of adverse events related to cosmetic procedures in all settings and falsely minimize the true potential for harm to patients.

Despite the recent attention focused on the rise of medical spas in aesthetic medicine, no formal studies have thoroughly examined their presence in the field in connection with their associated complications through a national survey of aesthetic practitioners. Our study aims to fill this gap in the literature by surveying members of the ASDS. Our results offer information and insights into how we can better educate practitioners and patients about the potential risks and dangers.

Materials and Methods

Online surveys were distributed via the Internet to current members of the ASDS as of 2019. Each individual was asked for demographic data, as well as their experiences interacting with and attitudes toward medical spas and associated complications.

Results

A total of 306 respondents completed the survey. There was a mean 13.9 years of experience working in aesthetic medicine. The majority worked in an urban setting (56.9%) compared with suburban (40.5%) and rural (2.6%) locations. For the vast majority (80.7%), the closest medical spa was <5 minutes away using typical transportation for the area.

In the past 2 years, the majority (70.3%) of respondents have had 1 to 20 patients experience cosmetic complications from medical spas. Of all cosmetic complications encountered in the past 2 years, the majority (63.1%) reported that the percentage of complications seen in their practice attributable to medical spas ranged from 61% to 100% (Figure 1).

The top 5 most cited cosmetic complications from medical spas were burn (89.7%), discoloration (80.1%), misplacement of product (74.6%), scar (69.4%), and bruise (52.9%) (Figure 2). The top 5 most cited treatments resulting in complications were fillers (80.4%), intense pulsed light (74.9%), laser hair removal (73.4%), neurotoxins (54.0%), and lasers for discoloration (50.5%) (Figure 3). The top 3 most cited reasons for why these complications may have occurred were improper training or education (90.0%), improper technique (88.3%), and improper device setting (77.3%).

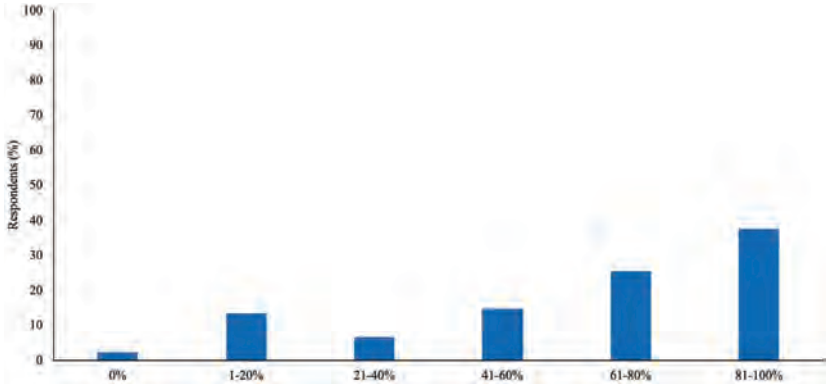


Figure 1. Percentage of all cosmetic complications in the past 2 years which were associated with medical spas.

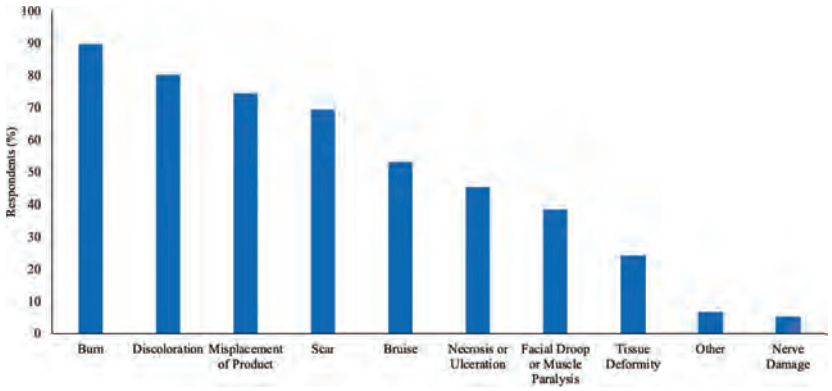


Figure 2. Types of cosmetic complications associated with medical spas.

When the training background of the medical director for the medical spa was known, the top 3 most cited specialties were family medicine (40.9%), obstetrics/gynecology (25.1%), and emergency medicine (23.7%). Interestingly, dermatology was the least cited (2.4%) (Figure 4).

Regarding safety, medical spas were rated by respondents to be worse than the average physician practice for fillers (97.6%), intense pulsed light (95.2%), skin tightening and resurfacing (94.3%), laser hair removal (91.3%), laser tattoo removal (89.6%), neurotoxins (80.9%), and body contouring (67.6%).

Regarding outcomes, medical spas were rated by respondents to be worse than the average physician practice for fillers (96.6%), skin tightening and resurfacing (92.0%), intense pulsed light (91.2%), neurotoxins (89.0%), laser tattoo removal (86.0%), laser hair removal (80.2%), and body contouring (69.6%).

The majority (58.8%) believed medical spas are either very or extremely endangering to patient safety. The majority (67.0%) was either not familiar with or only somewhat familiar with the rules and regulations, whereas 95.8% believed these should be stricter. Most respondents (84.3%) would like more information and support from medical societies.

Discussion

Demand for noninvasive and minimally invasive aesthetic procedures continues to grow at a remarkable pace. Medical spas have capitalized on this opportunity with over 5,400 facilities across the country in 2018, representing a total value approaching nearly $10 billion.[5] Many of these facilities are located in states that do not require direct physician oversight and are often managed by nurse practitioners, nurses, and naturopaths. A recent study demonstrated that the majority of medical directors possessed training backgrounds that were neither dermatology nor plastic surgery.[6] Interestingly, nearly 30% of the

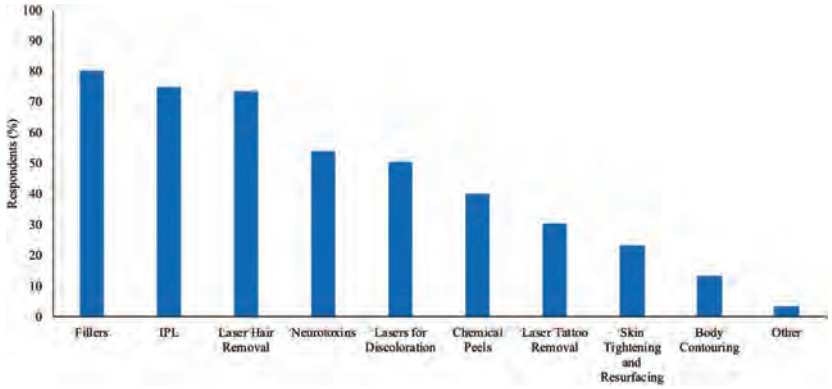


Figure 3. Sources of cosmetic complications associated with medical spas.

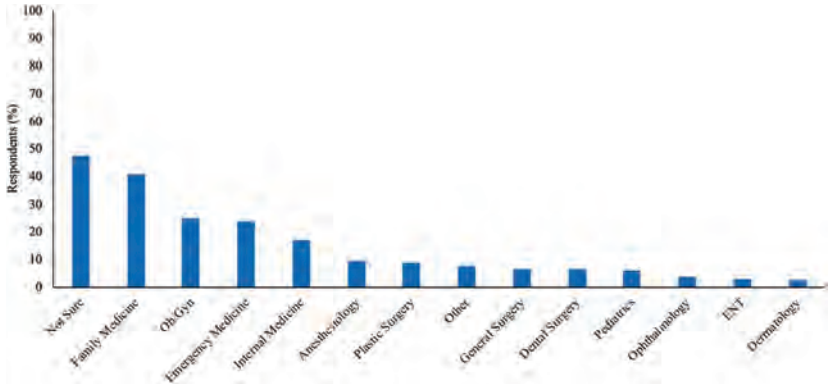


Figure 4. Training background of medical director for medical spa when complications were encountered.

interviewed medical spas had a medical director who did not perform any procedures themselves, and nearly half were off-site for the majority of the time. Inconsistent supervision and disparate state-by-state regulations coupled with the rapid expansion of medical spas have created a perfect storm for patient endangerment.

The majority of respondents had a medical spa within 5 minutes of their workplace, which is consistent with the recent expansion. An alarming majority also treated several patients who suffered a cosmetic complication from a medical spa. Furthermore, cosmetic complications from medical spas comprise a significant portion of complications treated by responding practitioners. Although this study certainly has recall bias due to the inherent nature of the survey, no other studies have yet to thoroughly examine these trends, and this study begins to shed light on this topic.

The survey attempted to address the systemic faults associated with medical spas that may be responsible for these adverse outcomes. Respondents suspected that the most common reasons for these complications may be improper training, technique, and device settings. However, the causes of complications were likely assumed in many cases. Further investigation into the background of the medical directors also revealed an interesting trend. The top 3 most cited specialties were family medicine, obstetrics/gynecology, and emergency medicine, whereas dermatology was by far the least cited at 2.4%. Interestingly, plastic surgery was cited at only 8.9%. Furthermore, the field continues to expand, and physicians from other specialties, such as general surgery and pediatrics, have ventured into the procedural aesthetic field.[7]

Expertise certainly plays an integral role in patient safety and outcomes. Very few specialties outside of dermatology and plastic surgery dedicate comparable clinical training to mastering skin pathology, anatomy, and medical and aesthetic treatments. A retrospective biopsy study found that dermatologists were more clinically accurate at diagnosing neoplastic and cystic lesions than nondermatologists, including family physicians, various surgeons, internists, and pediatricians.[8] Compounding these issues, physicians—dermatologists included—are increasingly delegating aesthetic procedures to physician extenders whose qualifications and training lack a universal standard.[9] To further highlight the associated dangers, numerous reports have begun to surface documenting the cosmetic referral of pigmented lesions that are ultimately diagnosed as melanomas.[10]

Regarding the safety and outcomes of common cosmetic procedures, respondents consistently rated medical spas as inferior to the average physician-based practice, especially for laser devices. However, these numbers may be somewhat skewed because practicing dermatologists may have an inherent bias. A recent study demonstrated that laser hair removal was the most commonly litigated procedure, with nonphysicians operating these devices 40% of the time.[11] From 2008 to 2011, the percentage of medical professional liability claims stemming from

cutaneous laser surgery performed by nonphysicians increased by nearly 115%, from 36.3% to 77.8%.[12] During the same time period, procedures performed by nonphysicians in medical spas represented almost 80% of lawsuits. Adequate training and proper treatment are vital to patient safety, and sufficient oversight can provide an additional layer of protection.

Nearly two-thirds of respondents reported that they were not familiar with or only somewhat familiar with current guidelines governing medical spas. Unfortunately, rules and regulations are not universal. There are nationwide variations in state medical board bylaws regulating the number of nonphysicians a single physician may supervise, the requirement of physicians to be on-site, and the extent to which delegation of procedural tasks may occur.[13] For these reasons, it is clear why most respondents desired more information and support from our field's medical societies. Additional advocacy on behalf of patients, consumers, and physicians is needed to regulate acceptable standards of care at medical spas across the country.

Conclusion

Patients who have experienced complications from medical spas are not uncommon in aesthetic dermatology. Overall, practitioners believe medical spas are endangering patient safety, think that stricter rules and regulations are necessary, and request more support from the specialty medical societies.

References

1. American Society for Dermatologic Surgery. *2018 ASDS Survey on Dermatologic Procedures*. 2018. Available from: https://www.asds.net/portals/0/PDF/procedures-survey-results-infographic-2018.pdf. Accessed August 15, 2019.
2. American Society for Dermatologic Surgery Association. *Position on Physician Oversight of Medical Spas*. Available from: https://www.asds.net/Portals/0/PDF/asdsa/asdsa-position-statement-physician-oversight-in-medical-spas.pdf. Accessed August 15, 2019.
3. American Academy of Dermatology Association. *Position Statement on Medical Spa Standards of Practice*. Available from: https://www.aad.org/forms/policies/uploads/ps/ps-medical%20spa%20standards%20of%20practice.pdf. Accessed August 15, 2019.
4. Alam M, Kakar R, Nodzenski M, Ibrahim O, et al. Multicenter prospective cohort study of the incidence of adverse events associated with cosmetic dermatologic procedures: lasers, energy devices, and injectable neurotoxins and fillers. JAMA Dermatol 2015;151:271–7.
5. American Med Spa Association. *2019 Medical Spa State of the Industry: Executive Summary*. Available from: https://www.americanmedspa.org/page/med-spa-statistics. Accessed August 15, 2019.
6. Gibson JF, Srivastava D, Nijhawan RI. Medical oversight and scope of practice of medical spas (med-spas). Dermatol Surg 2019; 45:581–7.
7. Housman TS, Hancox JG, Mir MR, Camacho F, et al. What specialties perform the most common outpatient cosmetic procedures in the United States? Dermatol Surg 2008;34:1–7.
8. Sellheyer K, Bergfeld WF. A retrospective biopsy study of the clinical diagnostic accuracy of common skin diseases by different specialties compared with dermatology. J Am Acad Dermatol 2005; 52:823–30.
9. Resneck JS Jr, Kimball AB. Who else is providing care in dermatology practices? Trends in the use of nonphysician clinicians. J Am Acad Dermatol 2008;58:211–6.
10. Stankiewicz K, Chuang G, Avram M. Lentigines, laser, and melanoma: a case series and discussion. Lasers Surg Med 2012;44: 112–6.
11. Jalian HR, Jalian CA, Avram MM. Common causes of injury and legal action in laser surgery. JAMA Dermatol 2013;149:188–93.
12. Jalian HR, Jalian CA, Avram MM. Increased risk of litigation associated with laser surgery by nonphysician operators. JAMA Dermatol 2014;150:407–11.
13. Choudhry S, Kim NA, Gillum J, Ambavaram S, et al. State medical board regulation of minimally invasive cosmetic procedures. J Am Acad Dermatol 2012;66:86–91.

Address correspondence and reprint requests to: Jordan V. Wang, MD, MBE, MBA, Department of Dermatology and Cutaneous Biology, Thomas Jefferson University, 833 Chestnut Street, Suite 740, Philadelphia, PA 19107, or e-mail: jordan.wang@jefferson.edu

Medical Spa or Physician Practice: The National Impact of Patient Wait Times in Aesthetics

The popularity of minimally and noninvasive procedures has recently risen. In an attempt to meet this demand, the medical spa industry has grown significantly. Although this has increased the accessibility of cosmetic procedures—often at significantly reduced prices—concerns include less stringent oversight and the potential for inferior patient outcomes. Compared with physician practices, medical spas may be more susceptible to deficiencies in training, improper technique, and incorrect device settings, which have been documented as probable causes for their adverse events.[1] Although complications occur in every office, the experience of aesthetic surgeons is that complications from cosmetic procedures frequently originate in medical spa settings.

Better understanding of the factors that contribute to consumer decision-making when choosing between cosmetic practice types may improve the overall safety of our field. A widely accepted belief is that patients often choose medical spas because of lower costs, but wait times may also play an important role. Although no studies have examined the potential influence of patient wait times, previous data has demonstrated that most aesthetic patients prefer to be seen within 1 to 2 weeks after calling for an appointment.[2] Our study aims to assess the differences in patient wait times between medical spas and physician practices to shed more light on this topic.

In January 2019, data for the 10 most populous cities in the United States were collected from a representative sample consisting of 5 each of medical spas, cosmetic dermatology practices, and plastic surgery practices. All reported practices answered questions. Wait time was determined for a new patient appointment via telephone call. For medical spas, additional information was gathered. Various local factors were examined.

Overall, mean wait times were 2.68 days for medical spas, 8.14 days for plastic surgery practices, and 10.76 days for cosmetic dermatology practices. Medical spas had significantly shorter wait times than plastic surgery practices ($p = .0002$) and cosmetic dermatology ($p = .0002$) practices. Medical spas also more frequently had same-day appointments available (10) compared with plastic surgery practices (4) and cosmetic dermatology practices (2).

The cities with the longest wait time for medical spas were San Diego (6), New York (3.8), Los Angeles (3.8), Houston (3.4), and Chicago and Philadelphia, which were tied (2.2) (Table 1). In comparison, the cities with the longest wait time for physician practices were San Jose (18.8), San Antonio (14.5), Phoenix (11.3), Dallas (11.3), and San Diego (10.4) (Table 1). For 9 cities, the wait time for medical spas was less than that of physician practices, whereas the remaining city (Chicago) was equal. The top 5 cities with the greatest difference in wait times between medical spas and physician practices were San Jose (17), San Antonio (12.5), Dallas (10.7), Phoenix (10.3), and Los Angeles (4.6) (Table 1).

Interestingly, there were no significant relationships between the overall combined wait times and number of medical spas in the city ($p = .2012$), number of physician practices in the city ($p = .2128$), number of all practice types combined in the city ($p = .1840$), population of the city ($p = .2949$), or median household income of the county ($p = .0507$).

For medical spas, the practitioner was reported to be a nurse (50%), physician (22%), nurse practitioner (14%), physician assistant (8%), and aesthetician (4%) (Figure 1). This had no significant association with wait time of the medical spa. The medical director was reported to be on-site for 46% of locations.

ISSN: 1076-0512 • Dermatol Surg 2020;00:1–3 •

ATTACHMENT D

TABLE 1. Patient Wait Times (Days) for Medical Spas and Physician Practices in Cities, Sorted by Differences in Wait Times Between Practice Types in Descending Order

City	*Wait Time for Physician Practices (Range)*	*Wait Time for Medical Spas (Range)*	*Differences in Wait Times Between Practice Types*
1. San Jose, CA	18.8 (0–75)	1.8 (1–4)	17.0
2. San Antonio, TX	14.5 (1–34)	2.0 (0–7)	12.5
3. Dallas, TX	11.3 (1–47)	0.6 (0–1)	10.7
4. Phoenix, AZ	11.3 (1–39)	1.0 (0–2)	10.3
5. Los Angeles, CA	8.4 (1–14)	3.8 (0–13)	4.6
6. San Diego, CA	10.4 (1–28)	6.0 (0–21)	4.4
7. Philadelphia, PA	6.3 (1–14)	2.2 (0–6)	4.1
8. New York, NY	6.4 (1–16)	3.8 (1–13)	2.6
9. Houston, TX	4.9 (0–24)	3.4 (0–6)	1.5
10. Chicago, IL	2.2 (0–9)	2.2 (0–6)	0.0

The medical director was a physician (62%), nurse practitioner (6%), physician assistant (4%), and nurse (2%) (Figure 1). Interestingly, staff was unsure of the background of the medical director for 26% of locations.

Although limited by sample size, the results demonstrate shorter wait times for medical spas compared with cosmetic dermatology and plastic surgery practices, which may influence the patient selection of procedural practice setting, and ultimately, impact patient care. Larger studies are needed to confirm these results. Studies have shown that when compared with physician practices, various procedures performed at medical spas were rated to be worse in both patient safety and outcomes.[1] Our results identified a physician as the on-site practitioner in less than a quarter of medical spas. Perhaps more alarming was the fact that medical directors—of whom only 62% were physicians—were on site for less than half of the locations. These findings corroborate a recent study, which demonstrated that about half of medical spas had their medical director on-site for less than 50% of the time.[3]

This inconsistent level of oversight at medical spas has likely contributed to higher rates of complications. Nowhere is this more apparent than in litigation studies, which serve as a proxy for poor patient outcomes in procedural cosmetics. From 2008 to 2011, the percentage of medical professional liability claims stemming from cutaneous laser surgery performed by nonphysicians increased by nearly 115%.[4] Procedures performed by nonphysicians in medical spas accounted for nearly 80% of lawsuits. These troubling numbers demand further investigation into how medical spas are regulated.

Among the cities in our study, 3 of their states require mandatory reporting of adverse events (California, Illinois, Texas).[5] In addition, California does not require on-site supervision, whereas Illinois requires it to only a certain extent. New York and Texas mandate

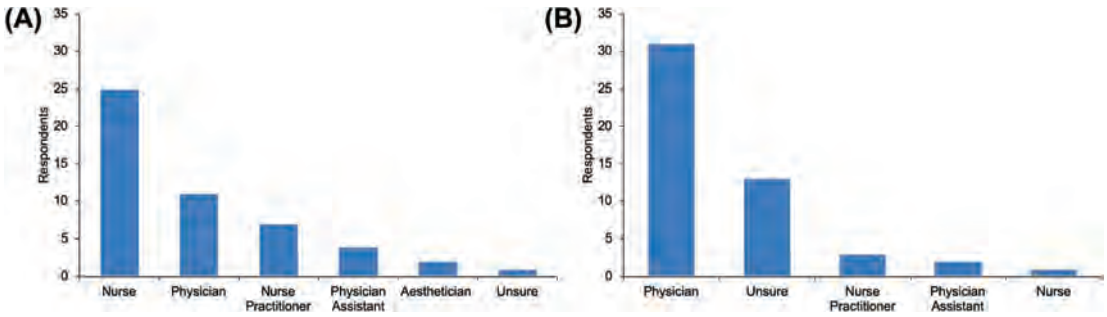


Figure 1. Background of (A) practitioner and (B) medical director for medical spas.

oversight, but at a physician's discretion. This wide range of regulation highlights the variable frameworks that medical spas operate within across state lines. Consequently, adverse events can go under-reported, and delegation to unqualified nonphysician practitioners may go unchecked.

Often times, patients may not be aware of the credentials and oversight of the performing practitioner, or even that a difference in outcomes may exist. Patients may also find it more convenient to schedule an appointment at a medical spa because of shorter wait times. Patients may have interest in being treated immediately, and therefore, select a medical spa over a physician-based practice. Additional studies should look into how wait times can influence consumer decision-making processes. These findings have important clinical implications, especially given stark differences in practice environments. Further attention should focus on the regulation of medical spas and the safety of our patients.

References

1. Wang JV, Albornoz CA, Goldbach H, Mesinkovska N, et al. Experiences with medical spas and associated complications: a survey of aesthetic practitioners. Dermatol Surg Epub 2020 Feb 11.
2. Wang JV, Zachary CB, Saedi N. Factors influencing consumer decisions in aesthetics: selection of procedures and practitioners. Dermatol Surg Epub 2019 Aug 6.
3. Gibson JF, Srivastava D, Nijhawan RI. Medical oversight and scope of practice of medical spas (med-spas). Dermatol Surg 2019;45: 581–7.
4. Jalian HR, Jalian CA, Avram MM. Increased risk of litigation associated with laser surgery by nonphysician operators. JAMA Dermatol 2014; 150:407–11.
5. Choudhry S, Kim NA, Gillum J, Ambavaram S, et al. State medical board regulation of minimally invasive cosmetic procedures. J Am Acad Dermatol 2012;66:86–91.

Jordan V. Wang, MD, MBE, MBA*
Saloni Shah, BS*
Christian A. Albornoz, MD*
Thomas Rohrer, MD†
Christopher B. Zachary, MBBS, FRCP‡
Nazanin Saedi, MD*
*Department of Dermatology and Cutaneous Biology
Thomas Jefferson University
Philadelphia, Pennsylvania
†SkinCare Physicians
Chestnut Hill, Massachusetts
‡Department of Dermatology
University of California
Irvine, Irvine, California

The authors have indicated no significant interest with commercial supporters.

ATTACHMENT D

https://www.arkansasonline.com/news/2019/jun/08/board-raises-doubts-over-spas-top-docto/

Board raises doubts over spas' top doctor

Infrequent visits, lack of training cited

June 8, 2019 at 2:03 a.m.

by Kat Stromquist

The medical director of two Northwest Arkansas aesthetics clinics has no training in many of those facilities' procedures and appears on-site at each once every other month, he told the Arkansas State Medical Board on Thursday.

During an appearance requested by the board, Dr. Donald Hill of It's a Secret Med Spa in Fayetteville and Rogers said he wasn't specifically trained in cosmetic techniques such as chemical peels, injecting dermal fillers or using intense pulsed light -- a treatment used to fight aging and skin discoloration -- while supervising nurses and techs who offer those services.

Hill said his work at the offices, which specialize in cosmetic services such as laser hair removal and Botox injections, is more focused on chart review and assessing potential contraindications.

"I don't see my role as someone who would actually perform the procedure," he said.

Board members were flummoxed by the situation, questioning the doctor's ability to oversee staff members and offer expertise in that context.

"It's hard for me to understand how you can be a medical director of a clinic ... when you haven't had any training in these procedures that they're performing," board member Dr. Rhys Branman said. "I find it very problematic that you are delegating procedures to individuals who are not trained to make medical diagnoses."

Learning that Hill visited each clinic approximately once every eight weeks, board members also expressed dismay at the infrequency of his visits while he estimated that 300-400 procedures were being done per month.

They said the situation puts those patients at risk and exposes Hill to legal jeopardy.

"Why would you stake your reputation and your name on this?" Dr. Brian Hyatt, another board member, asked Hill. "What do you think the outcome for you is, if one of these goes bad?"

Earlier in the meeting, Branman, who is a cosmetic surgeon, had outlined the risks of seemingly minor procedures such as dermal fillers, which can cause necrosis or blindness if administered improperly.

The board voted to call Hill back for a "show cause" hearing at its August meeting to determine whether he had violated the Arkansas Medical Practices Act, which regulates doctors' activities in the state.

ATTACHMENT D

Hill, whose specialty is listed as internal medicine, apologized to the board and said "I've realized that this is something I should not be doing. ... I will not continue to do this."

Information about the clinic's practices also will be forwarded to the Arkansas State Board of Nursing, as well as county sheriff's offices and the attorney general's office to look at whether the businesses ran afoul of the Arkansas Medical Corporation Act, board attorney Kevin O'Dwyer said.

It's a Secret Med Spa is a chain of clinics that includes several locations in Texas as well as two clinics in Arkansas, according to its website.

The company's director of operations declined to comment to the Arkansas Democrat-Gazette, and Hill didn't return a call Friday.

Metro on 06/08/2019

Received: 11 June 2020 | Revised: 13 July 2020 | Accepted: 24 July 2020

ATTACHMENT D

DOI: 10.1111/jocd.13645

COSMETIC COMMENTARY

JCD Journal of Cosmetic Dermatology

WILEY

Differentiation in a market of imitation: The evolving world of aesthetic dermatology

Jordan V. Wang MD, MBE, MBA[1,2] | Nazanin Saedi MD[1] | Roy G. Geronemus MD[2]

[1]Department of Dermatology and Cutaneous Biology, Thomas Jefferson University, Philadelphia, Pennsylvania

[2]Laser & Skin Surgery Center of New York, New York, New York

Correspondence
Jordan V Wang, MD, MBE, MBA, Laser & Skin Surgery Center of New York, 317 E 34th Street, 6th Floor Research Department, New York, NY 10016.
Email: drjordanwang@gmail.com

Abstract

This commentary examines the recent general movement in the field of cosmetic dermatology toward imitation and reproduction. The issues of medical spas, nonphysician operators, and counterfeit products have recently garnered interest in aesthetic dermatology. As physicians, it is our professional and bioethical responsibility to ensure that our patients are educated on the presence of medical spas, nonphysician operators, and counterfeit products in our field, especially given the discrepancies in patient safety and outcomes. There are also actions that dermatologists can take in order to help differentiate themselves in this current market. This will not only protect our field, but also our patients, who we are obligated to provide high-quality care for as physicians.

KEYWORDS

aesthetics, dermatology, lasers, marketing, patient safety

1 | INTRODUCTION

Over the past few decades, the field of aesthetic dermatology has continued to evolve. What was once considered a small subspecialty has now transformed into an independently flourishing field of its own. The popularity of cosmetic procedures has considerably increased, especially as minimally invasive procedures have captured the attention of patients. In such a rapidly expanding and highly profitable aesthetic market, dilemmas will inevitably develop. More recently, increased attention has focused on a general movement in our field toward imitation and reproduction. Aesthetic dermatologists should be aware of these current trends and strategies to help differentiate themselves as providers.

2 | MEDICAL SPAS

Medical spas have recently proliferated. In the most populous cities, they have even outnumbered cosmetic dermatologists and plastic surgeons.[1] Consumer interest has largely been fueled by persuasive marketing campaigns with particular emphasis on social media outreach. Unfortunately, the growth of medical spas has outpaced cosmetic dermatologists, which has likely been accelerated by disparate state regulations covering their oversight. Of all cosmetic complications encountered by members of the American Society for Dermatologic Surgery (ASDS) in the past 2 years, the majority reported that 61%-100% were attributable to medical spas.[2] These were believed to be the result of improper training and education, technique, and device settings. When examining litigation cases associated with nonphysician operators performing laser surgery from 2008 to 2011, nearly 80% of lawsuits originated from medical spas.[3] Some states are laxer than others (eg, allowing nurses or naturopaths to be medical directors, nonphysician operators to practice without physician supervision, and medical directors to be off-site), and there is relatively limited enforcement. Until the patchwork of state regulations are either more strictly reformed or unified, the proliferation of medical spas will likely continue.

Patients should be educated on the discrepancies in safety and outcomes between practice settings. Physicians can help to

differentiate themselves by openly advertising their expertise, and the dermatology clinic should promote itself as a physician-based practice. For example, all professional degrees and certifications should be visible in high-traffic areas, and any apparel, such as scrubs, should include professional credentials. The projected image of the physician should be consistent across all media platforms and outreach materials in order to convey a consistent message to patients.

3 | NONPHYSICIAN OPERATORS

Attempts to expand access to dermatologic care has led to an increase in physician extenders and technicians, who often perform cosmetic procedures.[4] Although they can work under the supervision of dermatologists, they have recently transitioned to settings where sufficient oversight can be an afterthought, such as salons, spas, shopping centers, personal homes, psychiatry offices, and dentistry offices. Even physicians who are not trained for aesthetic procedures and/or are from other specialties that are nonrelated to dermatology are playing an active role. In medical spas, physician extenders and aestheticians were the treating practitioner for 76% of locations, while medical directors were not even on-site for over half of the businesses.[5] These medical directors were often nonphysicians themselves, including nurses and physician assistants. Over the years, it has been argued that nonphysician operators lack the required expertise of physicians that comes from years of training and have a much higher turnover rate leading to additional training concerns of the replacement staff.

Cosmetic dermatology lends itself to many nuances that must be mastered—ideally through a formal certified training program, such as the ASDS-accredited Cosmetic Dermatologic Surgery Fellowship. Sufficient instruction can decrease adverse events and improve patient safety, especially in a field that has been exploited by less experienced providers practicing cookbook medicine. Aesthetic physicians should spread public awareness on the benefits of being treated by credentialed practitioners. They can also advertise their affiliations with academic institutions and memberships in professional societies, such as the ASDS. Societies have pushed for truth in advertising campaigns and clear communication of credentials, which is supported by the ASDS's model legislation for the Medical Spa Safety Act.[6]

4 | COUNTERFEIT PRODUCTS

The appearance of counterfeit products in aesthetics has garnered recent attention. In a 2019 survey, about 40% of aesthetic practitioners admitted to encountering them.[7] In terms of safety, 20.1% and 39.7% had encountered patients with adverse events from counterfeit medical devices and injectables, respectively. Nearly 1 in 20 practitioners purchased a counterfeit medical device, which doubled to 1 in 10 for injectables. Although often much cheaper, these products have not been formally tested using certified quality control measures and, therefore, offer no assurances of safety and efficacy to the practitioner and patient. Unfortunately, patients are unlikely to know when they are being treated with counterfeit products.

Aesthetic physicians should hold themselves to a higher standard and consider patient safety above other factors, including financial profits. They should only procure products from authorized retailers to avoid the inadvertent purchase of counterfeits, which was the case for nearly 80% of those who had bought counterfeit injectables.[7] Physicians should also be aware that secondary markets can sell devices from reputable brands, but these may not have received regular maintenance and/or may be ineligible for future service by the manufacturer. Physicians should warn patients when treatment with counterfeits is suspected by other practitioners. Additionally, they can directly show authentic products to patients, including packaging and labeling, prior to any procedure. This can help to train patients to request practitioners to do so in the future and can serve as an additional opportunity for patient education.

5 | CONCLUSIONS

In the ever-evolving world of aesthetics, consumers regularly fall victim to those who develop the best marketing strategies. Unfortunately, dermatologists are often unprepared and the least adept to fight this battle.[8] However, the real power of cosmetic physicians is in their education and training. They should ensure that their image and brand are appropriately portrayed to consumers to reflect this. This is the true voice of being a physician in the aesthetic field, and it should not be taken lightly. It is our professional and bioethical responsibility to ensure that patients are educated on the impact of medical spas, nonphysician operators, and counterfeit products in our field, especially given the stark differences in patient safety and outcomes. Although recent studies have begun to examine some of their dangers, additional studies are still needed in order to comprehensively evaluate their impact to our field and determine effective strategies to mitigate their risks. This will not only protect our field, but also our patients, who we are obligated to provide high-quality care for as physicians.

CONFLICT OF INTEREST

The authors have no relevant conflicts of interest to declare.

ORCID

Jordan V. Wang https://orcid.org/0000-0001-7437-2745

REFERENCES

1. Wang JV, Albornoz CA, Noell C, Friedman PM, Zachary CB, Saedi N. Skewed distribution of medical spas and aesthetic physician

practices: A cross-sectional market analysis. *Dermatol Surg*. 2020. [Epub ahead of print].
2. Wang JV, Albornoz CA, Goldbach H, et al. Experiences with medical spas and associated complications. *Dermatol Surg*. 2020. [Epub ahead of print].
3. Jalian HR, Jalian CA, Avram MM. Increased risk of litigation associated with laser surgery by nonphysician operators. *JAMA Dermatol*. 2014;150(4):407-411.
4. Resneck JS Jr, Kimball AB. Who else is providing care in dermatology practices? Trends in the use of nonphysician clinicians. *J Am Acad Dermatol*. 2008;58(2):211-216.
5. Wang JV, Shah S, Albornoz CA, Rohrer T, Zachary CB, Saedi N. Medical spa or physician practice: The national impact of patient wait times in aesthetics. *Dermatol Surg*. 2020. [Epub ahead of print].
6. American Society for Dermatologic Surgery. Model Legislation-Medical Spa Safety Act. <https://www.asds.net/Portals/0/PDF/asdsa/asdsa-medical-spa-safety-act.pdf>. Accessed 22 March 2020.
7. Wang JV, Hattier G, Rohrer T, Zachary CB, Saedi N. experiences with counterfeit aesthetic medical devices and injectables. *Dermatol Surg*. 2019. [Epub ahead of print].
8. Wang JV, Albornoz CA, Hazan E, Keller M, Saedi N. Business administration training for dermatology residents: Preparing for the business of medicine. *Clin Dermatol*. 2019;37(1):78-79.

How to cite this article: Wang JV, Saedi N, Geronemus RG. Differentiation in a market of imitation: The evolving world of aesthetic dermatology. *J Cosmet Dermatol*. 2020;00:1–3. https://doi.org/10.1111/jocd.13645

ATTACHMENT D

Original Investigation

Increased Risk of Litigation Associated With Laser Surgery by Nonphysician Operators

H. Ray Jalian, MD; Chris A. Jalian, JD; Mathew M. Avram, MD, JD

IMPORTANCE Controversy exists regarding the role of nonphysicians performing laser surgery and the increased risk of injury associated with this practice.

OBJECTIVE To identify the incidence of medical professional liability claims stemming from cutaneous laser surgery performed by nonphysician operators (NPOs).

DESIGN, SETTING, AND PARTICIPANTS Search of an online national database of public legal documents involving laser surgery by NPOs.

EXPOSURE Laser surgery by nonphysicians.

MAIN OUTCOMES AND MEASURES Frequency and nature of cases, including year of litigation, certification of provider and operator, type of procedure performed, clinical setting of injury, and cause of legal action.

RESULTS From January 1999, to December 2012, we identified 175 cases related to injury secondary to cutaneous laser surgery. Of these, 75 (42.9%) were cases involving an NPO. From 2008 to 2011, the percentage of cases with NPOs increased from 36.3% to 77.8%. Laser hair removal was the most commonly performed procedure. Despite the fact that approximately only one-third of laser hair removal procedures are performed by NPOs, 75.5% of hair removal lawsuits from 2004 to 2012 were performed by NPOs. From 2008 to 2012, this number increased to 85.7%. Most cases (64.0%) by NPOs were performed outside of a traditional medical setting.

CONCLUSIONS AND RELEVANCE Claims related to cutaneous laser surgery by NPOs, particularly outside of a traditional medical setting, are increasing. Physicians and other laser operators should be aware of their state laws, especially in regard to physician supervision of NPOs.

JAMA Dermatol. 2014;150(4):407-411. doi:10.1001/jamadermatol.2013.7117
Published online October 16, 2013.

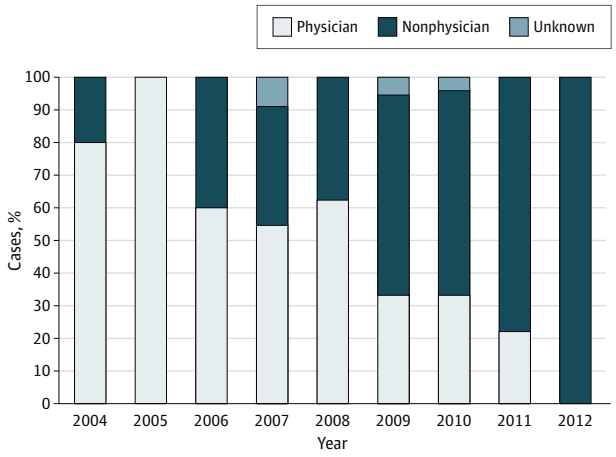
Author Affiliations: Division of Dermatology, University of California, Los Angeles (H.R. Jalian); Wellman Center for Photomedicine, Massachusetts General Hospital, Boston (H.R. Jalian, Avram); Paul Hastings, LLC, New York, New York (C.A. Jalian); Department of Dermatology, Harvard Medical School, Boston, Massachusetts (Avram).

Corresponding Author: H. Ray Jalian, MD, Division of Dermatology, University of California, Los Angeles, 2020 Santa Monica Blvd, Ste 570, Santa Monica, CA 90404 (hjalian@partners.org).

Cutaneous laser surgery remains one of the most popular elective procedures performed in the United States. Among dermatologic surgeons alone in 2011, more than 1.6 million laser treatments were performed.[1] Many more procedures were performed by physicians in other specialties and by nonphysician operators (NPOs). As the numbers of these procedures increase, a concomitant growth has occurred in laser injury-related litigation.[2] The practice of delegation to NPOs has accompanied the burgeoning trend toward greater availability of laser surgery and is hypothesized to be in part responsible for the increase in injury and litigation.[3] Moreover, the past decade saw the massive expansion of the so-called medical spas, nonmedical facilities offering aesthetic and cosmetic procedures.[4] Many of these facilities are owned by or retained by physicians; however, most of the procedures are performed by NPOs of varying certifications as permitted by state regulation. The degree of supervision varies among states, and often the physician supervisor is not required to be on the premises at the time of rendering of services.[5]

Many physicians are increasingly using physician extenders (PEs) within their practice to meet rising demand and falling reimbursements. Among dermatologists, almost 30% reported using a PE within their practice, a 40% increase over the preceding 5 years.[6] Although no data have emerged regarding increased litigation associated with this practice, legal precedence and numerous investigations are clear on liability.[7] When a physician delegates duties to a PE, responsibility and liability remain squarely on the supervising physician provided that the services rendered fall within the scope

Figure. Procedures Performed by Nonphysician Operators Increasingly Represent Most Lawsuits



The percentage of cases involving a nonphysician operator is expressed as a percentage of total operators per calendar year. Note the increasing trend toward a larger proportion of nonphysician operators starting in 2008.

of duty of the PE. This holds true for physician supervision of NPOs in the setting of cutaneous laser surgery.[2]

Despite these trends and clear inconsistencies in state regulations, no study to date has quantified the effect of these practices on medical professional liability claims with regard to cutaneous laser surgery. The objective of this study was to expand on previously published findings in an effort to identify high-risk practices that result in litigation. In addition, the study examines the incidence of litigation related to the performance of laser surgery by NPOs.

Methods

We searched the legal research resource WestlawNext (http://westlaw.com) using various keywords as previously reported.[2] This database is a primary source used by attorneys to gather legal information and is available by subscription to the public. Documents within this database are in the public record. The study was exempt from review, as determined by the institutional review board at Massachusetts General Hospital. An updated search yielded one additional case, bringing the total number of claims concerning injury resulting from cutaneous laser surgery to 175. Of these 175 cases, 75 of the procedures were performed by NPOs. For this study, an *NPO* is defined as a non-MD, non-DO provider. Because of the nature of the documents within the database, it is difficult to ascertain the exact certification of the NPOs. In an effort to be accurate, various allied health professionals comprised the NPO category. This included operators described as a *registered nurse* or a *nurse practitioner*, as well as terms such as *technician*, *aesthetician*, *assistant*, and *intern*. In addition to previously acquired data, the setting where services were rendered was recorded.

Results

NPO as a Function of Year of Litigation

Of 175 cases identified, the first occurrence of an NPO was in 1999. From January 1999, to December 2012, a total of 75 cases with NPOs were identified. This represents 42.9% of the total cases during the same time frame. Stratification of laser operator by year of litigation revealed a striking trend. From 2004 to 2012, a trend was observed toward an increased proportion of lawsuits stemming from cutaneous laser surgery performed by NPOs. This trend is most notable from 2008 to 2011, our most recent data, during which time the percentage of cases involving an NPO increased from 36.3% to 77.8%. Of the 2 cases in 2012, both were performed by an NPO. These results are summarized in the **Figure**.

Procedures

In line with our previously published data,[2] the most commonly performed procedure (n = 40) from 2004 to 2012 that resulted in injury and litigation by an NPO involved laser hair removal. Rejuvenation, composed mainly of intense pulsed light treatments, was the second most commonly litigated procedure (n = 7). Among the NPO cases, a notable trend is evident: when expressing the number of NPO cases as a percentage of the total number of cases for the same procedure, 75.5% of laser hair removal lawsuits from 2004 to 2012 were performed by an NPO. This number is even more dramatic in the years 2008 to 2012, when 85.7% of all laser hair removal lawsuits were performed by an NPO. From 2010 to 2012, a total of 90.0% (18 of 20) of laser hair removal cases were performed by an NPO. The remainder of the litigated procedures by NPOs and the proportion of total cases are given in **Table 1**.

Location of Services

From 1999 to 2012, a total of 64.0% (n = 48) of the NPO cases arose in a nonmedical practice setting. These include medical spas and other nonmedical facilities offering cosmetic services (eg, salons, spas, etc). In 2008 to 2011, NPO procedures performed in medical spas represented almost 80% of lawsuits. Of the 2 cases in 2012, one was performed in a medical spa setting and the other in a physician office. When looking at the type of procedure performed in this setting, most of these cases were laser hair removal procedures. From 2008 to 2012, a total of 68.6% (n = 24) of laser hair removal litigation cases involved an NPO in a medical spa setting. These results are summarized in **Table 2**.

Specific Allegations

Not surprisingly, the injuries sustained following laser surgery by NPOs and the causes of action in these cases mirror those previously reported by our group.[2] However, the specific allegations in these cases offer insight into various liabilities imposed on physician supervisors.

It is necessary to first examine the 2 different forms of liability (direct and vicarious) that a physician could face arising from allegedly improper laser treatment. A physician is directly liable for any negligence that can be attributed to an

ATTACHMENT D

Table 1. Cases Involving Laser Procedures Performed by Nonphysician Operators

Procedure	No./Total No. (%) All Cases[a] (n = 106)	All Cases by Nonphysician Operators 2004-2012[b]	All Cases by Nonphysician Operators 2008-2012[b]
Hair removal	40 (37.7)	40/53 (75.5)	30/35 (85.7)
Rejuvenation[c]	7 (6.6)	7/22 (31.8)	7/22 (31.8)
Leg veins	3 (2.8)	3/7 (42.9)	3/7 (42.9)
Vascular[d]	1 (0.9)	1/4 (25.0)	1/4 (25.0)
Tattoo	1 (0.9)	1/4 (25.0)	1/4 (25.0)
Scar	2 (1.9)	2/2 (100.0)	2/2 (100.0)
Pigmented lesion	1 (0.9)	1/1 (100.0)	1/1 (100.0)
Other[e]	2 (1.9)	2/3 (66.7)	2/3 (66.7)

[a] All cases from 2004 to 2012, including physician, nonphysician, and unknown operators.

[b] All nonphysician operator cases expressed as a percentage relative to the total specific procedure cases with all operators.

[c] Most with an intense pulsed light device.

[d] Includes treatment of vascular lesions and telangiectasia.

[e] Includes one case related to fat removal and one case of skin tightening.

Table 2. Setting of Cases Involving Laser Procedures Performed by Nonphysician Operators

Year	No./Total No. (%) Medical Spa	Physician Office	Unknown Setting	Laser Hair Removal[a]
1999-2012	48 (64.0)	25 (33.3)	2 (2.7)	33/48 (68.8)
2004-2012	41 (70.7)	16 (27.6)	1 (1.7)	29/40 (72.5)
2008-2012	36 (76.6)	11 (23.4)	0	24/35 (68.6)

[a] Number of cases performed by nonphysician operators in a medical spa setting relative to the total procedures performed by nonphysician operators in all settings.

individual capacity (ie, the personal failure to perform his or her duties at the requisite standard of care). A physician's duties often extend beyond the laser procedure; for instance, a physician may be directly liable for any negligent hiring, supervision, or training and so forth.

Conversely, a physician is vicariously liable for the negligence of his or her employees. A physician's vicarious liability is rooted in the doctrine of *respondeat superior* (Latin for "let the master answer"). This common law doctrine is often used to hold the employer responsible for the actions of his or her employees if and when the employee is acting within the scope of his or her employment. The rationale underpinning the application of vicarious liability to an employer is 2-fold. First, an employer has the ability and duty to control his or her employees. Second, presumably an employee is performing duties that will result in a benefit to the employer and in so doing is acting under the direction or authority of the employer. Therefore, in a medical malpractice context, a physician can be vicariously liable for the negligence of his or her subordinates, including nurses, NPOs, and other staff.

Almost all of the malpractice cases arising from the negligence of NPOs are coupled with vicarious liability claims against the employer, often a medical spa but at times a physician owner. Notably, 25 of 58 cases (43.1%) with NPOs from 2004 to 2012 represented instances in which no direct physician supervisor was identified. In these cases, the facility was often named as the defendant. As for a physician's direct liability in NPO cases, by far the most common specific allegation (n = 27) was failure to supervise the delegate. Failure to supervise represents the physician's failure to properly oversee the procedure. Failure to train and hire appropriate staff was the second most common specific allegation (n = 23). In addition to these allegations, negligent entrustment (n = 2) was alleged against the physician employers in their individual capacity. Negligent entrustment arises when one party (the entrustor) is held liable for providing another individual (the entrustee) with a potentially dangerous instrument. In this context, a physician can be held liable for providing an NPO with a laser if this instrument is used for a procedure that results in injury to a patient. The physician liability is predicated on the fact that a reasonable person in like circumstances would not have entrusted the NPO with the equipment. A summary of specific allegations (where available) relating to injury sustained as a result of laser surgery by NPOs from 1999 to 2012 includes the following: failure to properly hire, train, or supervise staff (n = 27); failure to properly perform treatment or operate a laser (n = 23); failure to conduct a test spot (n = 10); lack of a license to perform a procedure (n = 6); failure to recognize or treat an injury (n = 5); and negligent entrustment (n = 2). As can be seen from the foregoing definitions, a physician's direct liability is predicated on his or her negligence, not the negligence of his or her employee or agent.

Discussion

Physician delegation of laser surgery has grown significantly during the past decade. In addition, nonphysician-supervised NPO laser surgery is being performed legally in many states at nonmedical facilities. Data on the safety of NPO performance of cutaneous laser surgery are lacking in the medical literature. Most important, a clear trend demonstrates a dramatic increase in the number of lawsuits associated with NPO performance of laser surgery. The NPOs comprise a vast diversity of operators, including nurse practitioners, registered nurses, medical assistants, electrologists, and aestheticians, among others. In 2011, the latest year with a presumed complete data set, 77.8% of the cases involved an NPO. In addition, of the cases with NPOs, almost two-thirds occurred outside of a traditional medical practice. From an examination of

ATTACHMENT D

the specific allegations available in this study, the following 2 themes emerged: (1) both vicarious and direct liability of the supervising physician and (2) the prevalence of nonmedical personnel failing to perform procedures commensurate with the standard of care, including recognizing and treating complications.

We propose that the overall trend in increased litigation for laser surgery is in part explained by greater numbers of NPOs performing these procedures, in particular those practicing without direct supervision in the medical spas. This is the first study to date to offer such quantitative evidence. Of the procedures performed, laser hair removal accounted for most of these cases. Indeed, laser hair removal is the most frequently performed laser procedure in the United States.[8] However, if one takes into account the number of procedures performed by operators (physician vs NPO), the data become even more compelling. Only one-third of laser hair removal procedures in 2012 were performed by an NPO; the remaining two-thirds were performed by physicians.[8] Despite the fact that physicians perform most laser hair removal, 85.7% of laser hair removal lawsuits in our study from 2008 to 2012 are cases involving an NPO. In 2011, a remarkable 90.9%% (10 of 11) of laser hair removal litigation was against NPOs. One way to interpret these data is that some increased inherent risk of injury exists with an NPO.

The inconsistency and ambiguity of the state laws exemplify the lack of uniformity of the practice of delegation. For example, in Maine only a physician may operate a laser for hair removal. At the other end of the spectrum, Nevada as of June 2011 had no regulations regarding the use of a laser. In addition to the ability to delegate these procedures is the degree of supervision required. Some state statutes are explicit in stating the need for a written protocol, the requirement to appropriately train and document the training of personnel, and the necessity for adequate supervision. Many physicians "lend" their medical license to these facilities without meeting the legal requirements for supervision. In line with this, California recently passed a bill (California Assembly Bill 1548, Chapter 140) that increases penalties for illegally owning and operating a medical spa, with fines up to $50 000 and a maximum of 2 to 5 years in state prison. The lack of overarching federal law makes it difficult to uniformly require qualifications of personnel allowed to render laser treatments. Despite appropriate certification, regulations regarding appropriate training are ambiguous and are subject to interpretation. Because laws and regulations are constantly evolving, it is imperative for physicians who use PEs to be up to date. Current guidelines can be found at state medical board and state legislature websites.

In the correct setting, with close on-site supervision and appropriate training, the use of NPOs can prove to be a fruitful, productive, and safe environment for patients. Perhaps a larger issue is the role of NPOs, as well as physicians without adequate training, in the operation of a laser. Technology related to laser surgery has evolved rapidly since the description of selective photothermolysis by Anderson and Parrish[9] in 1983. Despite the propagation of nonmedical facilities performing these procedures, the tremendous amount of physics and medicine related to cutaneous surgery should not be overlooked. The American Society for Dermatologic Surgery Association position promulgates the use of energy devices capable of altering or damaging living tissue to physicians who are "trained appropriately in the physics, safety, and surgical techniques involved in the use of energy devices capable of damaging living tissue prior to performing procedures using such devices."[10] Moreover, in the setting of delegation, a physician "should be fully qualified by residency training and preceptorship or appropriate course work prior to delegating procedures to licensed allied health professionals and should directly supervise the procedures. The supervising physician shall be physically present on-site, immediately available, and able to respond promptly to any question or problem that may occur while the procedure is being performed."[10] Finally, the position statement underscores the need for "appropriate documented training in the physics, safety, and surgical techniques of each system. The licensed allied health professional should also be appropriately trained by the delegating physician in cutaneous medicine, the indications for such surgical procedures, and the pre- and post-operative care involved in treatment."[10]

Several limitations are inherent in conducting research using a legal database. First, although it is a massive data bank, only one legal database was searched. Cases within the database are those in which some form of legal action was taken and exclude complaints handled outside of the judicial system (ie, third-party arbitration through a malpractice carrier). This is likely to have excluded many frivolous claims with little merit. Second, the query was a retrospective review and was limited by the search terms selected; it is likely that some decisions exist that did not contain the searched terms. Third, these legal pleadings are layman documents (ie, not medical records), and the veracity of the facts was assumed to be true. Furthermore, layman terms may have eluded a database search for the purposes of this study. Fourth, because of the limited number of cases with NPOs for certain procedures, it is difficult to interpret the trends for less commonly performed surgery. Nonetheless, the actual data likely understate the true incidence of NPO laser complications. Generally, plaintiffs' attorneys do not pursue litigation against uninsured operators. Unlike physicians, NPOs (especially in a nonmedical office setting) are less likely to possess liability insurance that can satisfy a potential malpractice or other legal judgment.

A dramatic increase in litigation has been filed against NPOs performing cutaneous laser procedures in medical and nonmedical office settings. This has important implications for the safety of patients undergoing these procedures. When a physician delegates duties to a PE, responsibility and liability remain squarely on the supervising physician provided that the services rendered fall within the scope of duty of the PE. This holds true for physicians supervising NPOs in the setting of cutaneous laser surgery. Given the increase in NPO laser surgery procedures and a parallel trend in greater frequency of lawsuits, further studies are needed to examine this troubling trend in laser safety.

ARTICLE INFORMATION

Accepted for Publication: July 21, 2013.

Published Online: October 16, 2013. doi:10.1001/jamadermatol.2013.7117.

Author Contributions: Dr H. R. Jalian had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: H. R. Jalian, Avram.
Acquisition of data: H. R. Jalian, C. A. Jalian.
Analysis and interpretation of data: All authors.
Drafting of the manuscript: All authors.

Conflict of Interest Disclosures: Dr Avram serves as a member of the medical advisory board for Zeltiq Aesthetics, Inc, and of the scientific advisory board for Cytrellis Biosystems, Inc. He has served as a consultant for Unilever, Zeltiq Aesthetics, Inc, and Allergan within the past 12 months. No other disclosures were reported.

REFERENCES

1. American Society for Dermatologic Surgery. ASDS survey results demonstrate broad scope of practice for dermatologic surgeons. http://asds.net/_Media.aspx?id=6966. Accessed September 7, 2013.

2. Jalian HR, Jalian CA, Avram MM. Common causes of injury and legal action in laser surgery. *JAMA Dermatol*. 2013;149(2):188-193.

3. Brody HJ, Geronemus RG, Farris PK. Beauty versus medicine: the nonphysician practice of dermatologic surgery. *Dermatol Surg*. 2003;29(4):319-324.

4. International Spa Association. The U.S. spa industry: fast facts. http://experienceispa.com/media/facts-stats/. Accessed March 16, 2013.

5. Choudhry S, Kim NA, Gillum J, et al. State medical board regulation of minimally invasive cosmetic procedures. *J Am Acad Dermatol*. 2012;66(1):86-91.

6. Resneck JS Jr, Kimball AB. Who else is providing care in dermatology practices? trends in the use of nonphysician clinicians. *J Am Acad Dermatol*. 2008;58(2):211-216.

7. Nestor MS. The use of mid-level providers in dermatology: a liability risk? *Semin Cutan Med Surg*. 2005;24(3):148-151.

8. Press Center. Statistics. http://surgery.org/media/statistics. Accessed May 21, 2012.

9. Anderson RR, Parrish JA. Selective photothermolysis: precise microsurgery by selective absorption of pulsed radiation. *Science*. 1983;220(4596):524-527.

10. American Society for Dermatologic Surgery Association. American Society for Dermatologic Surgery Association position on the use of energy devices capable of altering or damaging living tissue. http://asdsa.asds.net/m/position/Laser-Procedures/. Accessed September 4, 2013.

NOTABLE NOTES

The Men or Women Behind Nevi: Alfred Guido Miescher

Fabrizio Vaira, MD; Gianluca Nazzaro, MD; Carlo Crosti, MD; Stefano Veraldi, MD

The man behind Miescher nevus is Alfred Guido Miescher. He was born on November 4, 1887, in Naples, Italy. His mother was Marietta Berner, and his father, Max Eduard Miescher, was a businessman. He was the nephew of Johannes Friedrich Miescher (1844-1895), professor of pathophysiology at the University of Basel, Switzerland, and discoverer of nucleic acids. After the father's death, he followed his mother to Basel, her hometown, where Guido completed his school.

He started his studies in engineering at the *Eidgenössische Technische Hochschule* in Zurich, Switzerland, and then switched to medicine, studying in Basel, Zurich, and Munich, Germany.[1] Working as an assistant of the dermatologist Bruno Bloch, he wrote his thesis on a case of mycetoma. In 1933, after the death of his mentor, Miescher become professor and director of the University Dermatology Clinic in Zurich. Miescher was an excellent clinician, and he was passionate about clinical dermatology and Dermatopathology. Indeed, he said that "Dermatology is more than morphology."[1]

In his original landmark work, *Histologie de 100 cas de naevi pigmentaires d'après les methods de Masson*, published in 1935, Miescher studied 100 hemispherical naevi found mostly on women's' faces. They are dome-shaped papules in which melanocytes are distributed mostly endophytically, often in a wedge, and they reach the deep reticular dermis.[2,3] Miescher was a pioneer in the treatment of skin diseases with phototherapy and of cutaneous tumors with ionizing radiation. Indeed, he helped to improve dermatological radiotherapy, through determining the safest doses and innovative fractionation schemes to reduce the toxic effects. Miescher was skilled in identifying new aspects of already known diseases. He reclassified granulomatosis disciformis chronica et progressiva, and, in 1945, he was the first to describe the cheilitis granulomatosa, subsequently also called Miescher cheilitis.

His students said that he cared about only 3 things: dermatology, music, and mountains. Miescher was a gifted cellist and a lover of mountaineering, as well as an illustrious dermatologist. He bravely climbed numerous Swiss peaks. But his most important venture was an expedition to the Caucasus Mountains. Miescher was the first person to climb Mount Elbrus (5629 m) and ski down. After a life full of medical and sporting achievements, he fought against the cancer and died in 1961.

Author Affiliations: Università degli Studi di Milano, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano, Italy.

Corresponding Author: Gianluca Nazzaro, MD, Dipartimento di Fisiopatologia Medico-Chirurgica e dei Trapianti, Università degli Studi di Milano–Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico–Milano, Italy, Via Pace, 9 Milano, Italy (gianluca.nazzaro@gmail.com).

1. Löser C, Plewig G, Burgdorf WHC, eds. *Pantheon of Dermatology: Outstanding Historical Figures*. Berlin, Germany: Springer; 2013.

2. Ackerman AB, Magana-Garcia M. Naming acquired melanocytic nevi: Unna's, Miescher's, Spitz's, Clark's. *Am J Dermatopathol*. 1990;12(2):193-209.

3. Fernandez-Flores A, Sanchez-Velicia L, Manjon JA, Alija A, Soto F. A hypothesis on the morphologic differences between Unna and Miescher nevi on the head and neck, based on embryologic bases. *Am J Dermatopathol*. 2012;34(6):602-606.

A Retrospective Analysis of Complications of Minimally Invasive Cosmetic Procedures Seen at a Referral Practice in Houston

There has been an unprecedented demand for minimally invasive aesthetic procedures in recent years.[1] According to the American Society for Dermatology Surgery, more than 4.1 million laser, light, or energy-based procedures were performed in 2019, a 106% increase over the previous 8-year period.[1] Dermatologists have always played a pivotal role in laser and cosmetic surgery innovation; however, there has recently been a proliferation of nondermatologists and medical spas offering advanced aesthetic treatments. Under the operation of experienced and well-trained cosmetic and laser surgeons, risk of complications is low, yet remains possible. As such, it is critical that those performing aesthetic procedures are well equipped to quickly identify and manage complications, should they arise.

Materials and Methods

A retrospective chart review of patients referred for burn and/or scar complications after minimally invasive and non-invasive aesthetic procedures at Dermatology and Laser Surgery Center in Houston, Texas, between 2012 and 2022 was conducted. Charts were reviewed for documentation of the procedure and device causing the complication as well as the provider or practice setting. The Fitzpatrick skin type (FST) for each patient was determined based on clinical documentation and supplemented with patient photographs. Patients were excluded if there was insufficient documentation of the procedure or if there were not any photographs of the affected area.

Results

Forty-two patients were identified as having procedure-related burn and/or scar complications with 38 patients meeting inclusion criteria. Thirty-two patients were treated with laser and light-based devices. Nine patients underwent facial resurfacing—5 with lasers and 4 with chemical peels. Two patients were treated with energy-based devices—1 with a radiofrequency device and 1 with cryolipolysis. Tattoo removal (23.7%) and resurfacing procedures (23.7%) were responsible for nearly half of the complications, followed by laser hair removal (21.1%), rejuvenation (15.8%), and treatment of vascular lesions (7.9%) (Figures 1–4). Treatment of pigmented lesions, skin tightening, and body contouring were each responsible for 2.6% of complications. Regarding the device, Q-switched lasers were responsible for most complications (26.3%) followed by IPL (intense pulsed light) (15.8%), CO_2 (10.5%) and chemical peels (10.5%). Diode lasers, long-

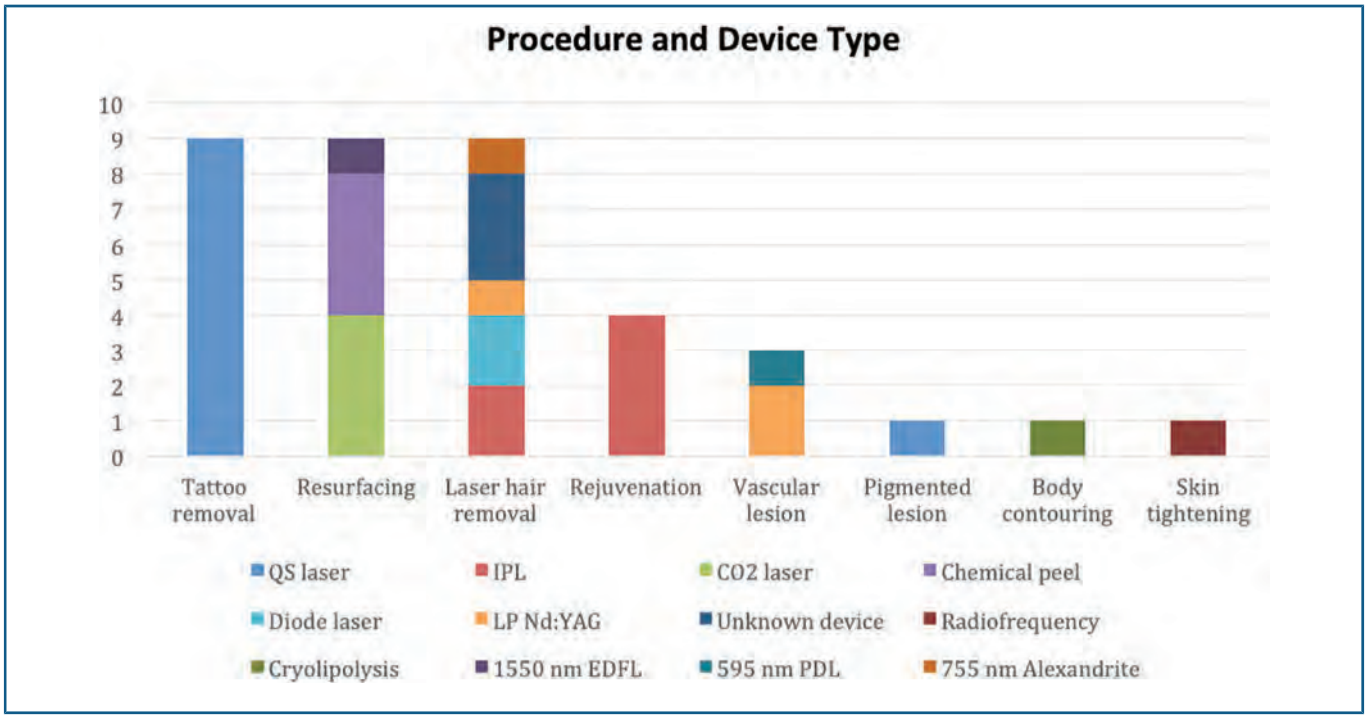


Figure 1. Cases per procedure type and device type. QS, Q-switched; IPL, intense pulsed light; Lp Nd:YAG, long-pulsed neodymium-doped:yttrium aluminum garnet; EDRL, erbium-doped fiber laser; CO_2, carbon dioxide; PDL, pulsed dye laser.

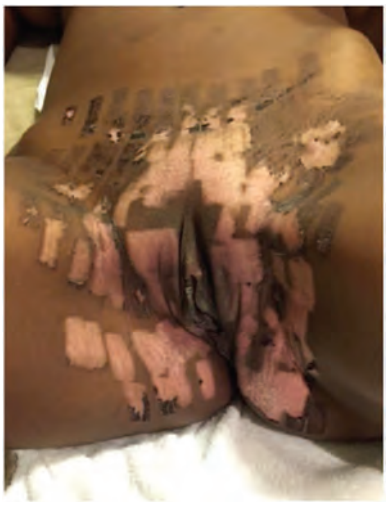


Figure 2. Burn after intense pulsed light treatment for laser hair removal.

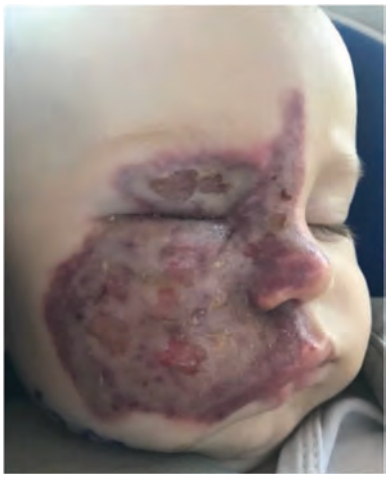


Figure 4. Inappropriate endpoint after pulsed dye laser treatment.

pulsed Neodymium-doped:yttrium aluminum garnet, and laser hair removal performed by an unknown device each accounted for 7.9% of complications. Radiofrequency, cryolipolysis, 1550-nm erbium-doped fiber laser, 595-nm pulsed dye laser, and 755-nm alexandrite laser were each responsible for 2.6% of complications. Fitzpatrick skin types included FST II (21.1%), FST III (36.9%), FST IV (18.4%), FST V (13.2%), and FST VI (10.5%). Complications most frequently arose from plastic surgery offices (34.2%) followed closely by medical spas (31.6%). Other providers implicated included dermatologists (5.3%), midlevels at dermatology offices (5.3%), other medical doctors (7.9%), and providers of unknown credentials (15.8%).

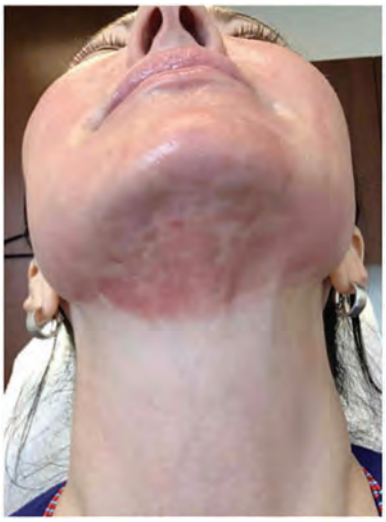


Figure 3. Hypertrophic scarring 4 weeks after cold atmospheric plasma with radiofrequency for skin laxity.

Other medical doctors included family medicine, general surgery, and obstetrics and gynecology.

Discussion

Given the rising popularity, it has become increasingly common for physicians across a broad range of specialties and midlevel practitioners to perform noninvasive and minimally invasive aesthetic procedures, often with little formal training.[2] This retrospective review demonstrated higher complication rates when these procedures are performed by medical spas, nondermatologists, and nonphysicians. Regarding devices, the greatest number of complications occurred after laser tattoo removal with Q-switched lasers at medical spas and laser clinics, likely because of laser tattoo removal clinics becoming franchised.[3]

For overall complications, medical spas ranked second to plastic surgeons who represented 31.6% and 34.2% of complications, respectively. The disproportionate number of complications from plastic surgeons could potentially be due to delegation of procedures to midlevels. Another possible explanation is that less time is spent learning minimally invasive aesthetic procedures during plastic surgery residency.[4] Other possible pitfalls include inadequate cooling, improper technique, and inappropriate patient, procedure, or settings.

Roughly 42% of complications occurred in patients with skin of color. Our findings show most complications occurred in FST III, which may result from practitioners using aggressive settings believing that the risk of complications is low. Before treating any patient, a thorough history and physical should be performed to assess for signs that may predict a higher risk of pigmentary changes or scarring conditions.[5] Although technological advancements have improved the safety and efficacy of many aesthetic procedures, complications are still possible and potentially devastating for

patients. In the future, we plan to report the senior author's experience in effectively managing these complications.

Limitations

Limitations include small sample size, cases obtained from a single center, and variability in documentation within the medical record.

Conclusion

Intimate knowledge of mechanism of action, device–tissue interaction, and clinical endpoints is imperative for all practitioners performing advanced aesthetic treatments to optimize patient outcomes while minimizing complications. Fitzpatrick skin type must also be taken into consideration when determining the appropriate procedure, device parameters, or strength of the peeling agent. As complications can arise even in capable and well-trained hands, all practitioners offering advanced aesthetic treatments must remain vigilant and be well versed in management of complications, should they arise.

References

1. American Society for Dermatologic Surgery. Survey on dermatologic procedures: report of 2019 procedures. Available from: https://www.asds.net/portals/0/PDF/procedures-survey-results-presentation-2019.pdf. Accessed November 13, 2022.
2. Valiga A, Albornoz CA, Chitsazzadeh V, Wang JV, et al. Medical spa facilities and nonphysician operators in aesthetics. *Clin Dermatol* 2022;40:239–43.
3. Karsai S, Krieger G, Raulin C. Tattoo removal by non-professionals–medical and forensic considerations. *J Eur Acad Dermatol Venereol.* 2009;24:756–62.
4. Morris MP, Toyoda Y, Christopher AN, Broach RB, et al. A systematic review of aesthetic surgery training within plastic surgery training programs in the USA: an in-depth analysis and practical reference. *Aesthet Plast Surg.* 2022;46:513–23.
5. Gold M, Alexis A, Andriessen A, Chilukuri S, et al. Supplement individual article: algorithm for pre-/post-procedure measures in racial/ethnic populations treated with facial lasers, nonenergy devices, or injectables. *J Drugs Dermatol.* 2022;21:SF3509903–11.

Taryn N. Murray, MD*
Nicole Salame, MD†
Paul M. Friedman, MD*‡§
**Dermatology and Laser Surgery Center, Houston, Texas*
†Department of Dermatology, Emory University School of Medicine, Atlanta, Georgia
‡Department of Dermatology, McGovern Medical School, University of Texas MD Anderson Cancer Center, Houston, Texas
§Department of Dermatology, Weill Cornell Medical College, Houston Methodist Hospital, Houston, Texas

The authors have indicated no significant interest with commercial supporters.

Fractional Er:YAG Laser and 0.01% Bimatoprost in Leucoderma From Iatrogenic Melasma Treatment in a Skin Phototype V Patient

Melasma has a chronic and recalcitrant nature. Most adverse effects that occur along the course of treatment are transient, except for scarring, exogenous ochronosis, and leucoderma. Leucoderma has been reported from topical hydroquinone and Q-switched neodymium-doped yttrium aluminum garnet (Qs Nd:YAG) 1,064-nm laser.[1,2] Treatment for leucoderma is often refractory and limited. To the best of our knowledge, treatment of leucoderma in melasma using fractional laser and bimatoprost has never been reported. We present a case of melasma with iatrogenic leucoderma successfully controlled with fractional erbium-doped yttrium aluminum garnet (Er:YAG) 2,940-nm laser in combination with topical 0.01% bimatoprost solution.

A 58-year-old Thai woman presented with facial melasma and leucoderma. She had melasma over the past 10 years and had been treated with topical medications, chemical peels, multiple sessions of Qs lasers, and unknown intralesional and intravenous injections from a private clinic. The patient stated that her melasma did not respond to previously prescribed topical agents such as AHA or whitening agents; however, it did respond to some procedural treatments but recurred afterward. Some white lesions gradually developed along the course of treatments. Physical examination revealed multiple well-defined guttate hypopigmented and depigmented macules with ill-defined irregular brownish patches on her face (Figure 1A). The patient has skin phototype V.

Initial treatment that we prescribed comprised a topical treatment that included 4% arbutin cream and 0.1% licorice PT40 cream for melasma and 0.1% tacrolimus ointment for leucoderma. After 6 months, no improvement was observed on both conditions. Fractional Er:YAG laser treatment was then considered. After 7 laser treatments, with an interval of 1 to 5 months (median 2.4) and a setting of 20 to 28 J/cm^2, 0.3-millisecond pulse width, 2% to 5% density, and 40 Hz, there was moderate improvement of melasma with the Melasma Area Severity Index (MASI) score reduction from 34 to 24 (29.4% improvement). For the melasma, the results were impressive considering the patient was a skin phototype V patient, and this skin type is known for a high chance of postinflammatory hyperpigmentation after procedures. However, only minimal repigmentation was observed on the leucoderma (Figure 1B).

To improve the leucoderma, fractional Er:YAG laser-assisted drug delivery with topical 0.01% bimatoprost solution (Lumigan; Allergan, CA) was considered.

ATTACHMENT D

INJECTABLES

RISKS AND COMPLICATION MANAGEMENT

Alabama Dermatology Society

ATTACHMENT D

CURRENT GROWTH OF MEDICAL SPAS IN THE U.S.

- Since 2010, number of nationwide medical spas has grown six fold
- In 2023, med spa industry in the US was projected to garner $20B in revenue, double from 4 yrs prior
- By 2025, annual revenue is expected to grow by 25% from 2023.
- Private equity in medical spas is at an all time high, expected to grow exponentially. Clinical knowledge is not a criteria they consider when purchasing a medical spa. They want multiple providers, MDs are not a draw for them and in face, quite the opposite.
- Only 37% of medical spas are owned by a physician, nurse practitioner ownership has doubled in 3 years
- Investors are diving in, starting or purchasing medical spas with the only objective being to sell in a few short years for a large profit. Medical spa industry is now more attractive than real estate for many investors.

ATTACHMENT D

RISKS OF ENLARGING THE MEDICAL SPA MARKET IN OUR STATE- TALES FROM OTHER STATES

A look at the state of Nevada

- Survey found that 75% of injectable treatments performed by nonphysicians
- Only 38% have an onsite physician
- Only 46% of complications are reported to the medical director, only 30% of which are core physicians
- Only 39.7% of surveyed spas had a number to call after regular business hours

Core physicians in other states are bombarded by complications from outside medical spas, causing many of them to refuse to see patients in need of care because of the risk of assuming liability for another injectors' complication.


Published in Dermatology
Journal Scan / Research · June 25, 2024

Assessing the Landscape of Supervision and Complication-Reporting in Medical Spas

Dermatologic Surgery


Who Is Holding the Syringe? A Survey of Truth in Advertising Among Medical Spas

Sara Hogan, MD, FAAD,* Emily Wood, MD, FAAD,† and Vineet Mishra, MD, FAAD, FACMS‡

ATTACHMENT D

RISKS OF SOFT TISSUE FILLER INJECTION

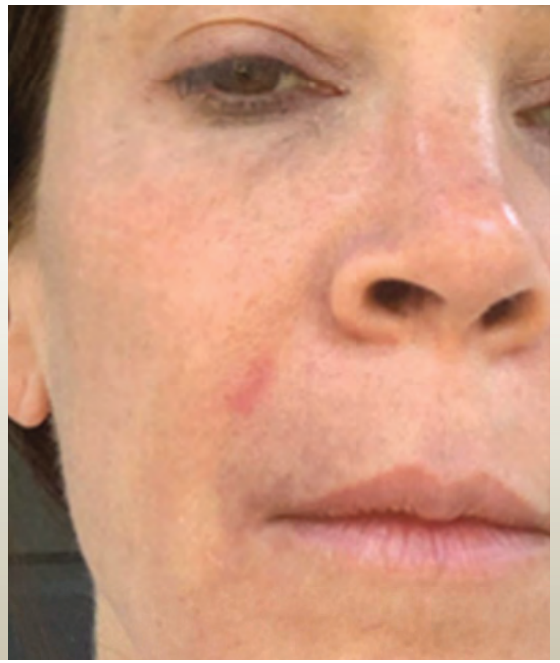
- Common risks: bruising, swelling, migration
- Less common: granulomas/allergic reaction, biofilm infection
- Rare but growing: vascular occlusions which may cause skin necrosis, blindness, stroke, death

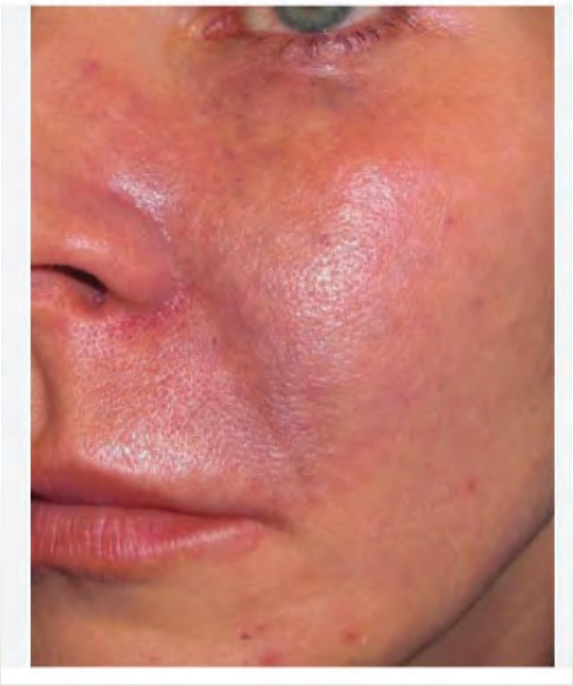
ATTACHMENT D

SKIN NECROSIS

Detection can be difficult, sometimes early findings are extremely subtle

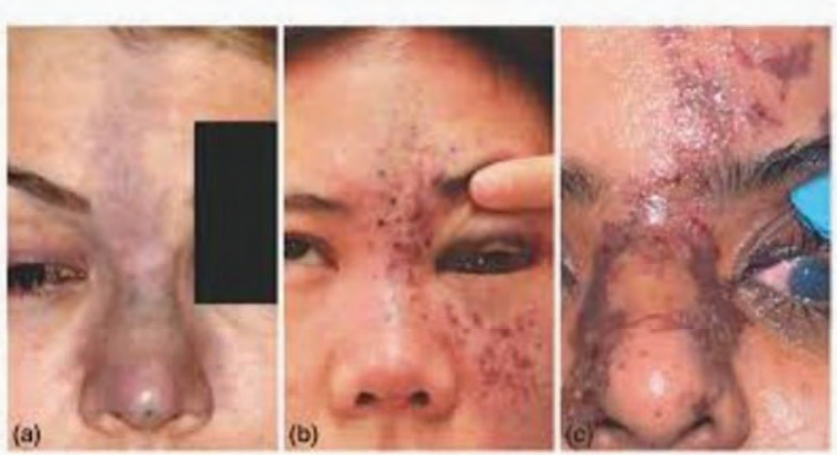
Even late findings can look like a bruise or shingles (commonly misdiagnosed)

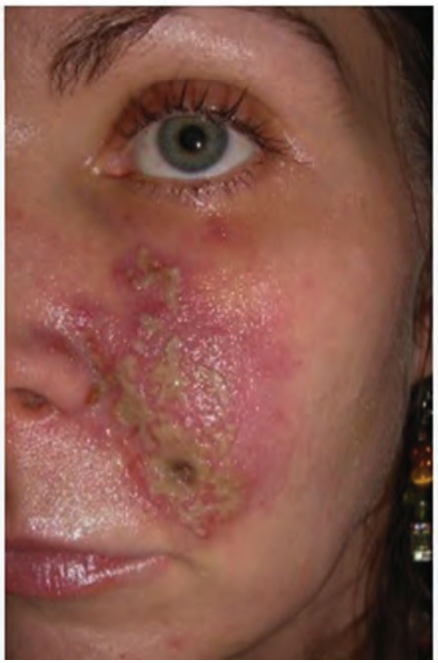


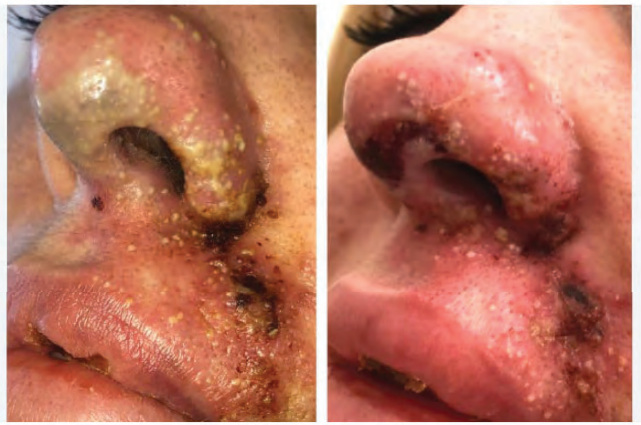


ATTACHMENT D

LATER STAGES OF VASCULAR OCCLUSION







ATTACHMENT D

BLINDNESS AND NEUROLOGIC COMPLICATIONS

Research article | Open access | Published: 18 July 2022

Sudden vision loss and neurological deficits after facial hyaluronic acid filler injection

Alexandra Lucaciu, Patrick Felix Samp, Elke Hattingen, Roxane-Isabelle Kestner, Petra Davidova, Thomas Kohnen, Jasmin Rudolph, Andreas Dietz, Helmuth Steinmetz & Adam Strzelczyk

Neurological Research and Practice **4**, Article number: 40 (2022) | Cite this article

Fig. 4

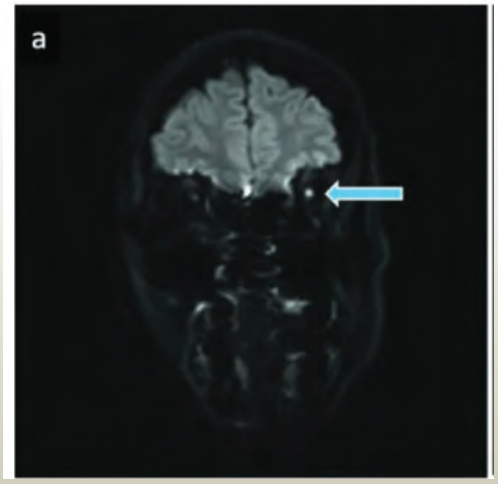
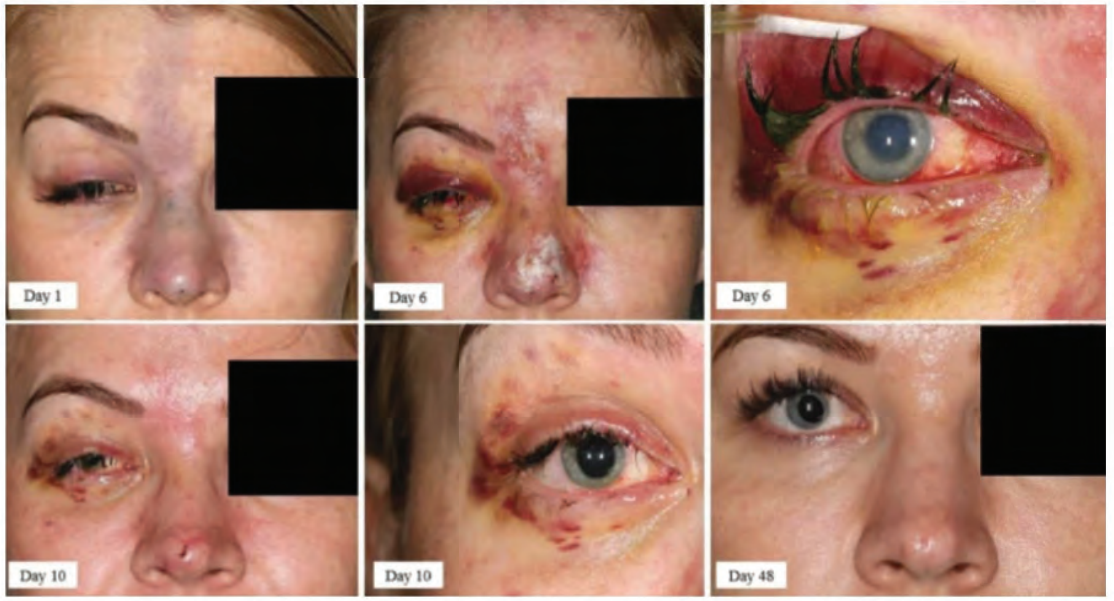


Fig. 5



ATTACHMENT D

VASCULAR OCCLUSIONS

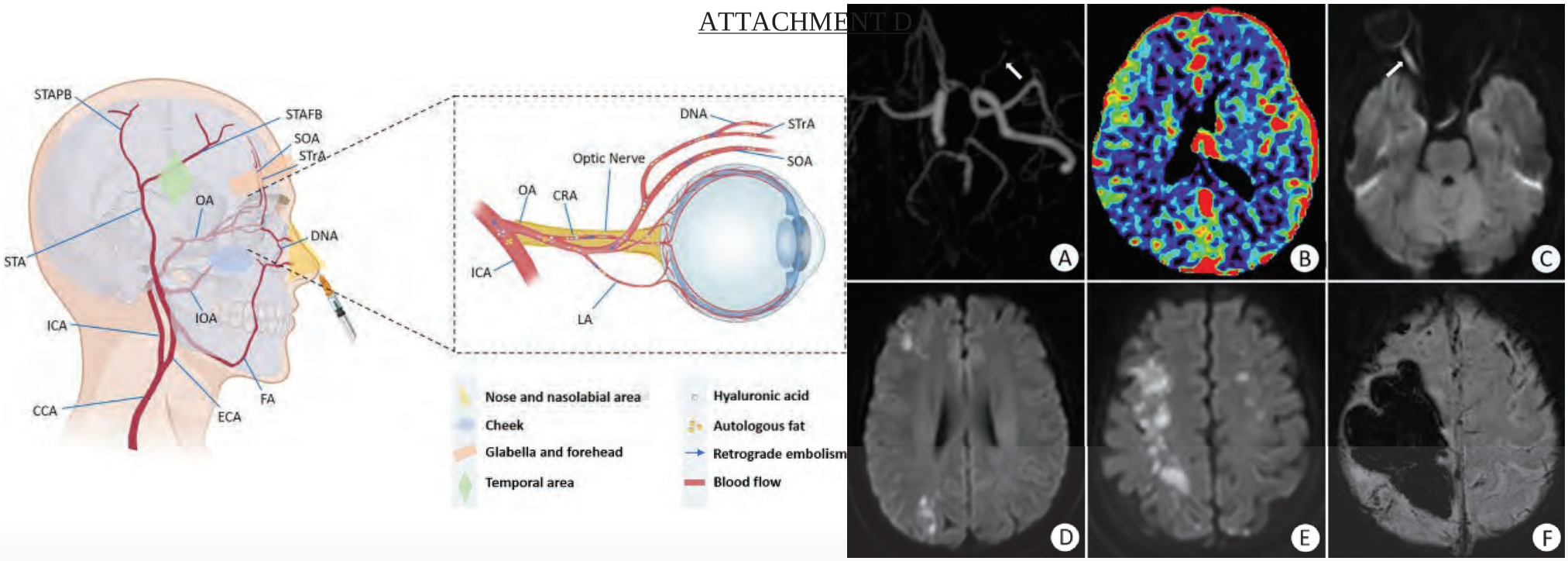
Comparative Study > JAMA Dermatol. 2021 Feb 1;157(2):174-180.
doi: 10.1001/jamadermatol.2020.5102.

Rates of Vascular Occlusion Associated With Using Needles vs Cannulas for Filler Injection

Murad Alam [1 2 3], Rohit Kakar [4], Jeffrey S Dover [5 6 7], Vishnu Harikumar [1 8], Bianca Y Kang [1], Hoi Ting Wan [1], Emily Poon [1], Derek H Jones [4]

- 37 dermatologists with average of 22.3 years in practice surveyed
- Cannula (1 in 40,882) has 77.1% lower odds of occlusion than needles (1 in 6410)
- MDs injecting longer than 5 years had 70.7% lower odds of occlusion

ATTACHMENT D



Visual loss and neurologic manifestations can occur when an instrument passes through or is lodged in an artery on the face, enough pressure is applied to overcome blood pressure (easy when injecting a gel through a needle), and plug embolizes to internal carotid system through multiple anastomoses with external carotid system.

ATTACHMENT D

1900-JAN 2015
98 CASES

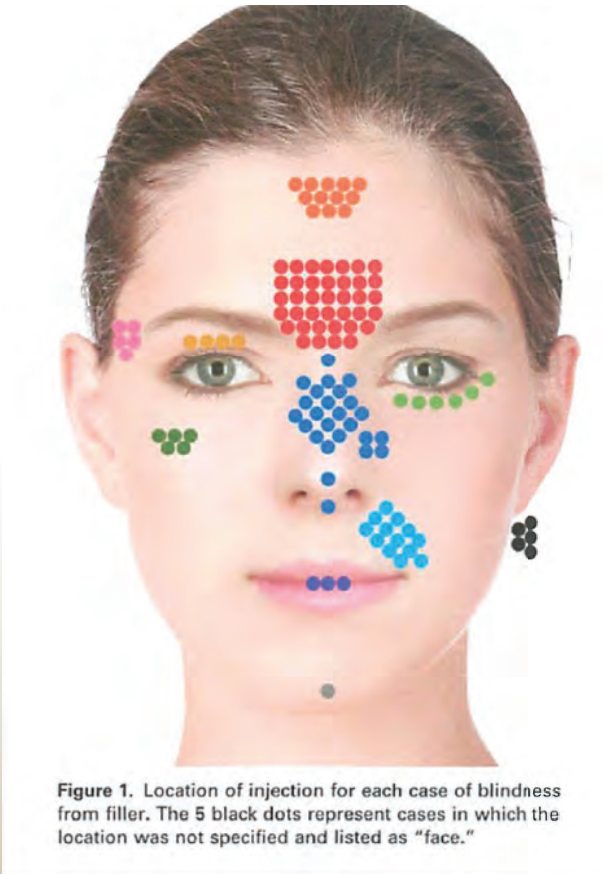


Figure 1. Location of injection for each case of blindness from filler. The 5 black dots represent cases in which the location was not specified and listed as "face."

Fat 47
HA 23
Other 38

Jan 2015-Sept 2018
48 cases

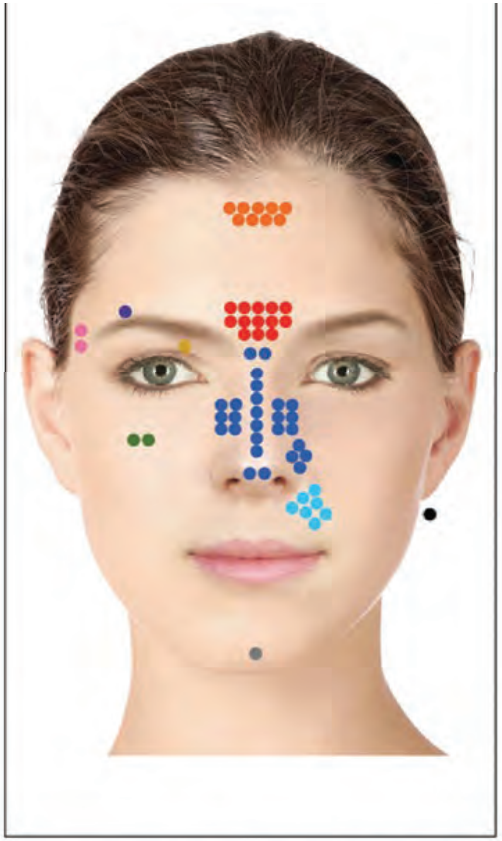


Figure 1. Location of filler injection resulting in visual complication. The single black dot represents a case where the anatomic location of injection was not specified.

Fat 1
HA 39
Other 8

Total cases
As of fall 2023

Approximately 350-400 cases but very underreported

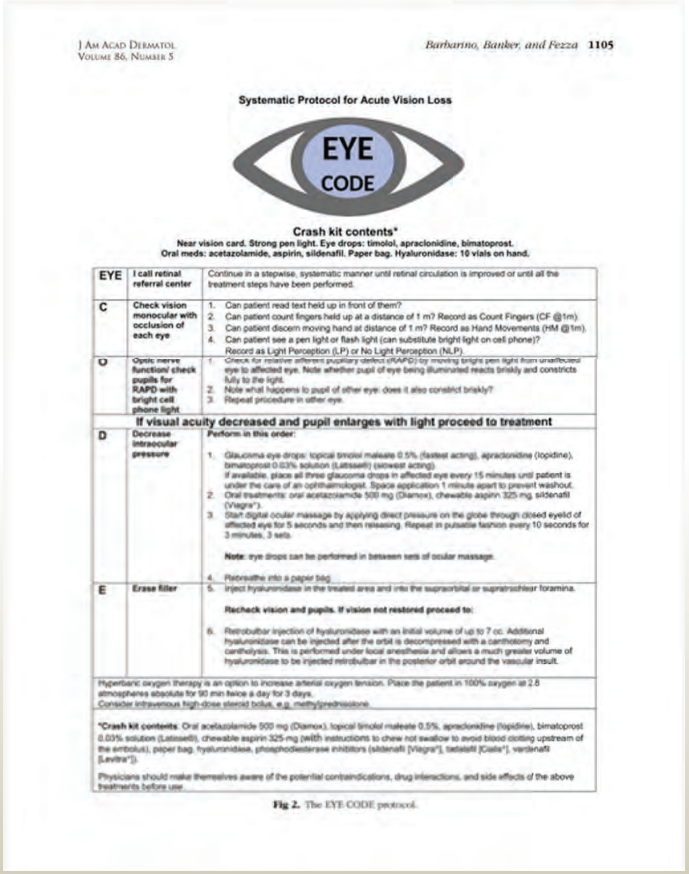
ATTACHMENT D

EYE CODE PROTOCOL DEVELOPED BY DERMATOLOGISTS

Published May 2022 in the Journal of the American Academy of Dermatology

Needed on site:
10 vials hyaluronidase
Timolol and bimatoprost eye drops
Oral acetazolamide, sildenafil, aspirin

Needed prior to occurrence:
Protocol including a retinal specialist within 20 minutes to perform possible retrobulbar hyaluronidase or alternatively IV antithrombotic



Systematic Protocol for Acute Vision Loss

EYE CODE

Crash kit contents*
Near vision card. Strong pen light. Eye drops: timolol, apraclonidine, bimatoprost.
Oral meds: acetazolamide, aspirin, sildenafil. Paper bag. Hyaluronidase: 10 vials on hand.

EYE	**I call retinal referral center**	Continue in a stepwise, systematic manner until retinal circulation is improved or until all the treatment steps have been performed.
C	**Check vision monocular with occlusion of each eye**	1. Can patient read text held up in front of them? 2. Can patient count fingers held up at a distance of 1 m? Record as Count Fingers (CF @1m). 3. Can patient discern moving hand at distance of 1 m? Record as Hand Movements (HM @1m). 4. Can patient see a pen light or flash light (can substitute bright light on cell phone)? Record as Light Perception (LP) or No Light Perception (NLP).
O	**Optic nerve function/ check pupils for RAPD with bright cell phone light**	1. Check for relative afferent pupillary defect (RAPD) by moving bright pen light from unaffected eye to affected eye. Note whether pupil of eye being illuminated reacts briskly and constricts fully to the light. 2. Note what happens to pupil of other eye: does it also constrict briskly? 3. Repeat procedure in other eye.
	If visual acuity decreased and pupil enlarges with light proceed to treatment	
D	**Decrease intraocular pressure**	**Perform in this order:** 1. Glaucoma eye drops: topical timolol maleate 0.5% (fastest acting), apraclonidine (lopidine), bimatoprost 0.03% solution (Latisse®) (slowest acting). If available, place all three glaucoma drops in affected eye every 15 minutes until patient is under the care of an ophthalmologist. Space application 1 minute apart to prevent washout. 2. Oral treatments: oral acetazolamide 500 mg (Diamox), chewable aspirin 325 mg, sildenafil (Viagra®). 3. Start digital ocular massage by applying direct pressure on the globe through closed eyelid of affected eye for 5 seconds and then releasing. Repeat in pulsatile fashion every 10 seconds for 3 minutes, 3 sets. **Note**: eye drops can be performed in between sets of ocular massage. 4. Rebreathe into a paper bag.
E	**Erase filler**	5. Inject hyaluronidase in the treated area and into the supraorbital or supratrochlear foramina. **Recheck vision and pupils. If vision not restored proceed to:** 6. Retrobulbar injection of hyaluronidase with an initial volume of up to 7 cc. Additional hyaluronidase can be injected after the orbit is decompressed with a canthotomy and cantholysis. This is performed under local anesthesia and allows a much greater volume of hyaluronidase to be injected retrobulbar in the posterior orbit around the vascular insult.
Hyperbaric oxygen therapy is an option to increase arterial oxygen tension. Place the patient in 100% oxygen at 2.8 atmospheres absolute for 90 min twice a day for 3 days. Consider intravenous high-dose steroid bolus, e.g. methylprednisolone.		
*Crash kit contents. Oral acetazolamide 500 mg (Diamox), topical timolol maleate 0.5%, apraclonidine (lopidine), bimatoprost 0.03% solution (Latisse®), chewable aspirin 325 mg (with instructions to chew not swallow to avoid blood clotting upstream of the embolus), paper bag, hyaluronidase, phosphodiesterase inhibitors (sildenafil [Viagra®], tadalafil [Cialis®], vardenafil [Levitra®]). Physicians should make themselves aware of the potential contraindications, drug interactions, and side effects of the above treatments before use.		

Fig 2. The EYE CODE protocol.

ATTACHMENT D

NURSING CORE CURRICULUM

- Foundations of Nursing: Introduction to nursing principles, ethics, and the role of the nurse.
- Health Assessment: Techniques for assessing patients' physical and mental health.
- Pharmacology: Study of drugs, their actions, and their use in treating illnesses.Pathophysiology: Understanding the physiological processes of diseases.
- Medical-Surgical Nursing: Care for adults with various medical conditions.
- Pediatric Nursing: Nursing care for infants, children, and adolescents.
- Maternal and Newborn Nursing: Care for pregnant women, newborns, and their families.
- Mental Health Nursing: Nursing care for individuals with mental health disorders.
- Community and Public Health Nursing: Focus on population health and preventive care.
- Nursing Leadership and Management: Preparation for leadership roles within nursing.

ATTACHMENT D

FALSE ADVERTISING AND ONLINE COURSES

SKIN GLOW DERMATOLOGY

Yelena Terushkin, PA-C

Overall Rating

★★★★★ 4.90

Skin Glow Dermatology is proud to be home to one of the best dermatologists in Brooklyn, Yelena Terushkin, PA-C. Renowned for her

ATTACHMENT D

MAJOR TAKE HOME POINTS FOR ALABAMA

- If injections are put in the hands of non MDs, we will see an increase in complications and patient harm. Injectables and thus, complications, will go up exponentially.
- When greedy investors see that the number of injectors is increasing by several fold which would occur if this resolution is passed, Alabama will become the “Medispa Gold Rush” state, with medical spas owned and operated by MDs with no experience, NPs, and PAs. They will all be hoping to “sell” in 3-4 years to these undesirable private equity groups for a lucrative deal. The fact that this market is untapped will make it very attractive for these undesirable groups.
- Acting responsibly after this passed, Alabama would need to put immediate rules in place for training, assessment of skill and knowledge levels, continuing education requirements, and monitoring and accountability. This would be more detailed, burdensome, and controversial than the laser rules changes from 2022-23 by a significant margin.

ATTACHMENT D

ALABAMA DERMATOLOGY SOCIETY
Committed to Excellence in Dermatology for Alabama

P.O. Box 43212
Birmingham, Alabama 35243
www.alabamaderm.org

December 2, 2024

Alabama Board of Medical Examiners
Mr. William Perkins, Executive Director
848 Washington Ave,
Montgomery, AL 36104

Dear Distinguished Members of the Alabama Board of Medical Examiners,

We respectfully thank you for allowing us to comment upon the recent Guidelines for Nurse Injectors. **Our primary concern for patient safety prompts us to adamantly oppose any rule that allows nurse practitioners, nurses, or physician assistants to inject dermal fillers.**

Over the past 10 years, an increase in all dermal filler injections and related complications has been well documented in the literature [1-9]. The most serious of these are ischemic complications including tissue necrosis, stroke, blindness, and death [1-9]. As this phenomenon becomes better understood, it has become more important than ever for all injectors to have a detailed knowledge of injection anatomy, years of experience in dermal filler injection, and a keen understanding of the sometimes subtle presentation of an ischemic event. Injectors should possess the correct tools available to manage an emergency situation and a commitment to maintain an education in the latest literature in this rapidly changing landscape [18]. The most important factor in the ultimate outcome of these ischemic complications is the timeframe in which they are diagnosed and treated [16,17,18].

While medical spas and other non-physician offices provide easier access such as shorter wait times, lower prices, and a less rigorous clinical environment [15], these "clients" often become new patients to dermatologists when complications occur and cannot be managed properly by the original injector [11]. In fact, many patients with complications from injection visits never return to the provider that caused them, creating an ongoing perception of safety among inexperienced injectors [Zhou et al]. In addition, the companies that distribute dermal fillers have a vested interest in lowering the bar for entry into this field, lulling potential injectors and patients into a sense of comfort [13] and creating a perception that dermal fillers are safe [11,13]. Unfortunately, these complications have exponentially increased in incidence across the United States as non-physicians have gained the ability to inject. These emergency complications, when unrecognized and mishandled, result in much more morbidity and, in some cases, mortality than is acceptable.

Furthermore, the medical spa industry has not penetrated our state the way it has in others. If non-physicians become injectors, greedy investors will identify Alabama as a new investment opportunity. Medical spas, who are owned and operated by non-medical private equity investors, untrained physicians, physicians assistants, nurse practitioners, and nurses, will multiply in Alabama [medspa.org REF1]. If the only requirement for ownership is an MD, Alabama will experience the tragic "absent medical director" situation that occurs nationally. Investors will hire suboptimally trained individuals hoping to grow profits and "sell" in 3-4 years to large private equity groups for a lucrative payout. The fact that this market is untapped will make it very attractive for these undesirable groups.

ATTACHMENT D

Acting responsibly after this passed, Alabama would also need to put immediate rules in place for training, assessment of skill, testing of knowledge, continuing education for maintenance, complication monitoring, and adverse event accountability processes, as well as rules regarding the acquisition of injectable products (how and where they are acquired). This would be burdensome, expensive, extremely time-consuming, and difficult to enforce in a way that ensures the safety of patients. With no reporting rules, no requirement other than an MD to be a medical director, and no formal training program in place, Alabama is simply not ready to take this on. **It is of particular note that dermatologists in this state are not requesting that access be granted to non-physicians, even though there would be potential financial benefit to them.**

Like you all, our organization cares deeply about health disparities in Alabama, not Botox disparities. When we are not defending patient safety, our organization funds rural residency training, increases primary care access to dermoscopy, and provides sun shades to schools--to name a few. We are all painfully aware that Alabama ranks poorly among common indicators of public health such as life expectancy and obesity [U.S. Dept of Health, 2023]. Advanced practice providers often cite this need for increased access to primary care in their arguments for scope changes [Hudspeth et al]. We do not understand how this request achieves that goal and, further, we fear it will shunt advanced practice providers away from primary care and toward Medical Spas [medspa.org ref2].

As always, we remain committed to providing open conversation and to engaging in thoughtful and purposeful solutions in our collective priority of patient care and safety.

Respectfully,
Submitted by the Alabama Dermatology Society Leadership

References

Zhou, Albert E., et al. “Ethics of Dermatologists Having to Manage Cosmetic Complications by Other Clinicians.” Journal of the American Academy of Dermatology., 2024, https://doi.org/10.1016/j.jaad.2024.07.1465.
https://americanmedspa.org/blog/selling-your-medical-spa

National Vital Statistics Reports, Vol. 73, No. 7, August 21, 2024; Centers for Disease Control and Prevention. Adult Obesity Prevalence Maps. U.S. Dept of Health and Human Services; 2023

Hudspeth et al, Understanding Nurse Practitioner Scope…JAANP, August, 2019

https://americanmedspa.org/blog/private-equity-and-growth-capital-medical-aesthetics-new-reality

ATTACHMENT D

December 2, 2024

William M. Perkins
Executive Director
Alabama Board of Medical Examiners
848 Washington Avenue
Montgomery, AL 36104

RE: Oppose Botulinum Toxin A and Dermal Fillers for Cosmetic Purposes Scope of Practice Expansion

Dear Mr. Perkins:

On behalf of the American Academy of Dermatology Association and the American Society for Dermatologic Surgery Association representing more than 17,000 dermatologists nationwide, we are writing to share our concerns with proposals that request the Alabama Board of Medical Examiners to authorize certified registered nurse practitioners (CRNP), physician assistants (PA) and registered nurses (RN) to administer botulinum toxin A and dermal fillers for cosmetic purposes.

Procedures by any means, methods, devices or instruments that can alter or cause biologic change or damage the skin and subcutaneous tissue constitute the practice of medicine and surgery. This includes the use of foreign or natural substances by injection or insertion. [i,ii] Our organizations believe that medical procedures using a Food and Drug Administration (FDA)-regulated device, such as those that can alter or cause biologic change or damage, should only be performed by a physician or appropriately trained non-physician personnel under the direct, onsite supervision of an appropriately trained physician.[iii] These proposals jeopardize patient safety and disregard what is considered adequate and appropriate medical education and training. Quality patient care includes evaluating a patient's needs and condition(s), selecting an appropriate course of treatment and providing adequate follow-up care.

With the growing public demand for facial fillers and neuromodulators, providing patients with properly trained, educated, and supervised medical personnel is a safeguard Alabama should have for its citizenry. Fillers and neuromodulators can also be used to treat scars from injury and surgery, as well as from medical conditions; other applications include correcting facial asymmetries resulting from congenital, accidental, or medical conditions. Our utmost concern is to ensure that these products are safely administered by licensed and qualified physicians or under the direct, on-site supervision of a licensed and qualified physician. "As with other cutaneous procedures, it is necessary to receive adequate training before using soft-tissue augmentation agents. Physician injectors should first be made to demonstrate a detailed knowledge of anatomy and possible adverse events (such as sensitivity, infection, and necrosis) through passing an American Board of Medical Specialties (or an ABMS-equivalent Board) examination in one of the CORE aesthetic specialties after residency training in one of these disciplines." [iv]

There are substantial differences in the education of non-physicians and physicians, both in depth of knowledge and length of training. Board certified dermatologists diagnose and treat over 3,000 different diseases and conditions. Dermatologists see patients of all ages – from newborns to the elderly. A board certified

dermatologist undertakes a minimum of 8 years of exhaustive medical education and training (4 years of medical school, 1 year of internship, 3 years (minimum) of dermatology residency), during which they complete 12,000 to 16,000 hours of direct patient care, before they can practice independently. Dermatologists must pass 3 standardized USMLE training exams to become licensed physicians and then pass a comprehensive examination at the conclusion of their residency training to become board certified in dermatology. Dermatologists have focused training in using fillers and neuromodulators involving the skin and adjacent structures, which prepares them to perform medical procedures using fillers and neuromodulators safely and effectively. Included in this training is proper technique, and the management of any adverse events.

In contrast, non-physicians have less clinical experience than a physician obtains in just the first year of a three-year medical residency. CRNPs obtain 500 to 720 hours of direct patient care, and PAs obtain 2,000 hours of clinical rotations after completing a 26-month program. These rotations emphasize primary care in ambulatory clinics, physician offices and acute or long-term care facilities.[v] Unlike physicians, non-physicians are not required to complete a residency program or demonstrate competency in procedures involving skin and soft tissue augmentation with products that can alter or damage living tissue. It is of upmost importance that the physician or non-physician performing procedures with neurotoxins (such as botulinum toxin) or dermal fillers have specific, long-term training (such as a medical residency in dermatology or plastic surgery). The education for non-physicians does not include this type of intense training; additionally, any short-term training program offered by manufacturers of these products does not adequately protect patient safety.

During a 2021 meeting of the FDA's General and Plastic Surgery Committee on Soft-Tissue Fillers, the American Society for Dermatologic Surgery's Task Force on Soft-Tissue Fillers found that knowledge of vascular anatomy is *crucial* for all filler injections. **Intravascular injection is possible at any location on the face, but certain locations carry a higher risk, such as filler embolization; necrosis; visual abnormalities; blindness; and stroke.**[vi] Thus, we are in firm agreement with the FDA's further updated consumer guidance in 2023 that anyone considering a neurotoxin or dermal filler consult with a licensed provider who is experienced in injecting dermal fillers, knowledgeable about fillers, anatomy, managing complications and knows the risks and benefits of treatment.[vii] Furthermore, the American Medical Association (AMA) states that, "Cosmetic medical procedures, such as botulinum toxin injections, dermal filler injections, and laser and intense pulsed light procedures, be considered the practice of medicine."[viii]

To best protect the citizens of Alabama from adverse events and ensure quality patient care, **we respectfully ask that the Alabama Board of Medical Examiners oppose the request to expand the scope of practice of CRNPs, PAs and RNs to include the administration of botulinum toxin A and dermal fillers for cosmetic purposes.** Thank you for your strong consideration on this matter. Should you have any questions regarding this critical patient safety issue, please do not hesitate to contact Kristin Hellquist, Chief Advocacy Officer at the American Society for Dermatologic Surgery Association, at khellquist@asds.net.

Sincerely,

American Academy of Dermatology Association
American Society for Dermatologic Surgery Association

---

[i] ASDSA *Position Statement on the Practice of Medicine*. https://www.asds.net/Portals/0/PDF/asdsa/asdsa-position-statement-definition-of-the-practice-of-medicine.pdf

[ii] AADA *Position Statement on Medical Spa Standards of Practice*. https://www.aad.org/Forms/Policies/Uploads/PS/PS-Medical%20Spa%20Standards%20of%20Practice.pdf

[iii] ASDSA *Position Statement on Delegation*. https://www.asds.net/Portals/0/PDF/asdsa/asdsa-position-statement-delegation.pdf

[iv] Gladstone H, Cohen J. Adverse Effects When Injecting Facial Fillers. Semin Cutan Med Surg. 2007 Mar;26(1):34-9.

[v] How are PAs Educated and Trained? https://www.aapa.org/what-is-a-pa/#tabs-2-how-are-pas-educated-and-trained

ATTACHMENT D

[vi] Jones D, Fitzgerald R, Cox S, Butterwick K, et al. Preventing and Treating Adverse Events of Injectable Fillers: Evidence-Based Recommendations From the American Society for Dermatologic Surgery Multidisciplinary Task Force. Dermatol Surg 2021;47:214-26.
[vii] Filling in Wrinkles Safely. Accessed Aug. 6, 2024. Retrieved from https://www.fda.gov/ForConsumers/ConsumerUpdates/ucm049349.htm
[viii] Addressing Safety and Regulation in Medical Spas. Retrieved Aug. 6, 2024. https://policysearch.ama-assn.org/policyfinder/detail/dermal%20fillers?uri=%2FAMADoc%2Fdirectives.xml-0-1174.xml

ATTACHMENT D

The New York Times

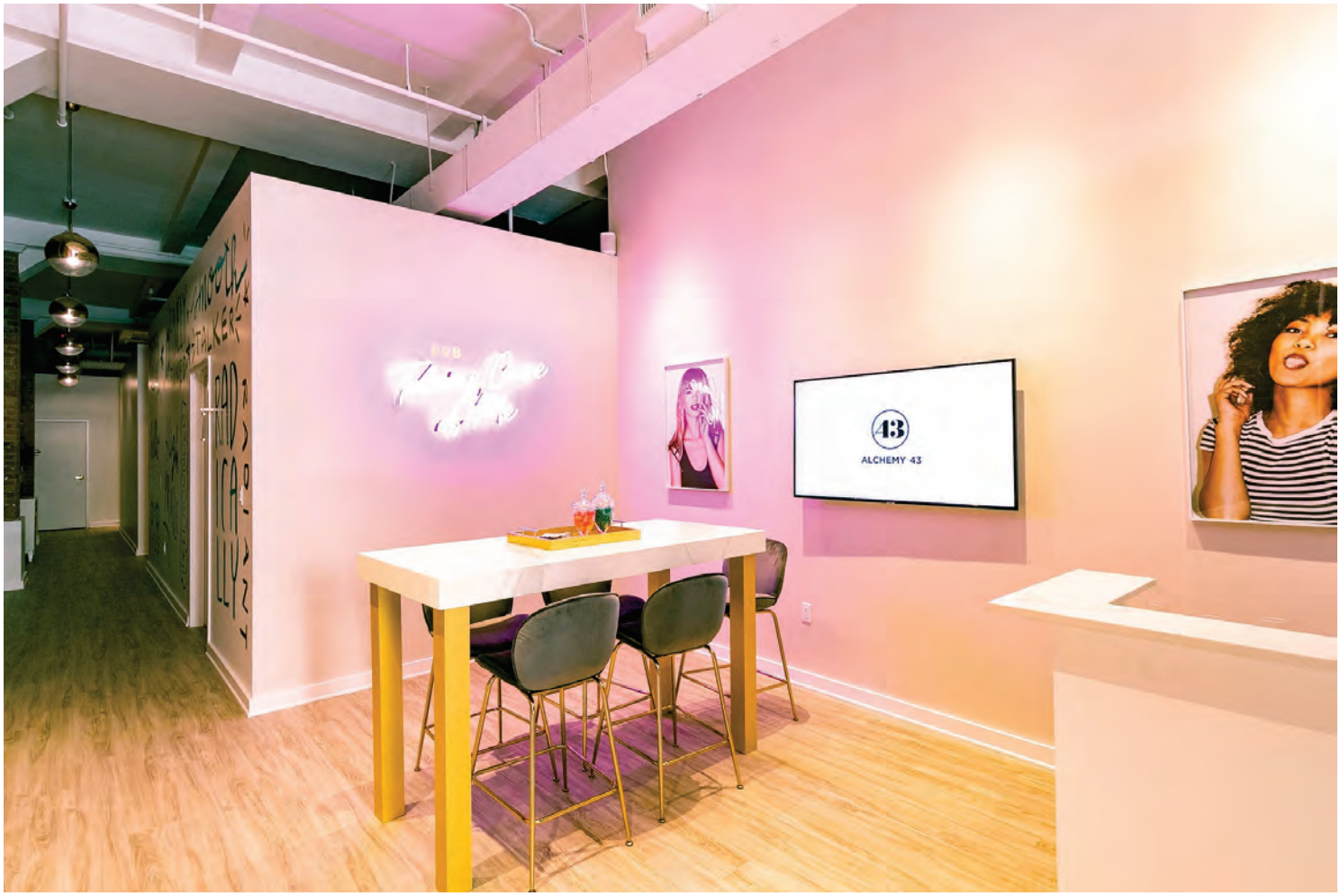
SKIN DEEP

Are You Ready for Drive-Thru Botox?

A new wave of beauty bars aims to make injectables as easy as a Drybar blowout.

By Courtney Rubin

April 30, 2019



Alchemy 43, newly opened in the Flatiron district. Jeenah Moon for The New York Times

There's nothing secretive about getting Botox and fillers at Ject in the West Village.

ATTACHMENT D

The three-month-old injectable beauty bar has a glass front with its name hand-painted in 23-karat gold. Treatment spaces are separated only by curtains. There's a photo booth, with a swirly gold, black and green mural that incorporates the company name, for customers who want to show off their freshly filled faces on social media. As the company recently Instagrammed: "Adieu, Taboo."

Indeed.

In 2018, injections of Botox — the No. 1 aesthetic procedure since 1999, according to the American Society of Aesthetic Plastic Surgery — were up 16.3 percent from the year before. Fillers were up 12 percent in the same time frame. Both procedures require regular top-ups.

With that popularity comes, almost inevitably, a wave of places that specialize in these injections, aiming to make them as accessible (walk-ins welcome!), acceptable and fun (in name, if not in needle) as a Drybar blow-dry.

A treatment room at Alchemy. Jeenah Moon for The New York Times

"Injectables don't need to be scary, and they don't need to be done in a secret garage," said Gabrielle Garritano, a physician assistant and a founder of Ject. The curtains, she said, were a choice, to make the place feel more salon, less medical office — and so clients may see others getting injected.

"You see people getting their hair blown out," she said, as if the two are equivalent.

ATTACHMENT D

Ject — the short name was chosen, in part, so it would look better on the forthcoming booking app — has plenty of competition. At Plump, in Chelsea, which is designed to look like a bistro, with dark wood floors, bar stools and a tea bar (serving anti-inflammatory elixirs), patrons can choose the $1,099 “Instaready Cheeks” or $240 “Goodbye Gummy Smile.”

They can then pose in front of an art installation of empty Botox vials or a millennial pink (the company calls it “Plump pink”) mural, where a small sign nearby reads: “Great art is meant to be shared. So are great results.” There’s even a prop: a pink board with letters spelling out “I Got Plumped.”

ATTACHMENT D

The menu board at Plump in Chelsea. Jackie Molloy for The New York Times

A second location will open on the Upper East Side in May, and there are plans for NoLIta, then Miami, where the founder Dr. Alexander Blinski (he prefers “Dr. B”) grew up.

Alchemy 43, which has four cucumber-and-lime-scented locations in Los Angeles, opened in the Flatiron neighborhood on April 24. The company, which says it has raised more than $5 million in funding, including from the Drybar founders, provides clients with fruit-garnished sparkling water in champagne flutes (pre-procedure alcohol is not recommended), and has a granite tabletop co-working space in the lounge. (À la Drybar, Alchemy also offers memberships.)

And BotoxLabb (the double Bs stand for “beauty bar”), a sea-foam-green-bathed chain based in Miami from the founders of the 1990s makeup brand Joey New York, is eyeing New York after introducing sea foam green outposts in Scottsdale, Ariz., and Los Angeles.

The company says that most of its clients are younger than 35, and many say they like the atmosphere of these places, and the focus on injectables.

Madeline Whaley, 29, an executive assistant in Beverly Hills, Calif., spotted an ad for Alchemy 43 (there are 43 muscles in the face, some researchers say) on Facebook and made the switch from a dermatologist.

ATTACHMENT D

Inside Plump. Jackie Molloy for The New York Times

“At the doctor’s office they know what they’re doing, but I always got the feeling it’s not their highest priority,” said Ms. Whaley, who gets Botox and fillers. “They spend a long time with you at Alchemy, and you feel really catered to.”

She has a $99-a-month membership, which gets saved up, as in a bank account, for her use; members also receive gift cards and, after a year, a free treatment, like lip or cheek filler, worth about $700. (Prices are generally cheaper than at a doctor’s office.)

According to the company, Alchemy customers spend an average of $475 per visit, and that figure is rising. As part of an initial consultation, Alchemy offers a 3-D sneak preview of what each treatment will look like on a client’s face.

Because of it, those who come in for the upper half of the face — eyes, forehead, cheekbones — often end up adding lower face treatments, said Nicci Levy, the company’s founder. (Ms. Levy formerly worked for Allergan, the maker of Botox, for which she was the highest-volume-selling representative. Her territory was just three blocks in Beverly Hills, ZIP code 90210.)

No matter the beauty bar of choice, that first shot of Botox can be a gateway drug. Every consumer interviewed for this article acknowledged multiplying treatments, and wanting to ramp up frequency.

“It’s so addicting,” said Olivia Grubman, 30, a resident in obstetrics and gynecology at Mount Sinai Hospital who started with Botox at Ject and then accessorized with cheek fillers. “Now if I see the tiniest little wrinkle on my forehead, I’m like, ‘I’ve got to go back.’”

ATTACHMENT D

At Ject, in the West Village. Jackie Molloy for The New York Times

On a recent Friday night, Dr. Grubman collected 10 friends (male and female) for an injectables party at Ject. As guests nibbled vegan desserts from Jack's, the Botox virgins got their treatments first to blunt the nervous anticipation.

Afterward, the party moved across the street to the Happiest Hour for drinks. Those with cheek fillers were perhaps marginally less happy. "When you laugh, it feels sore, but it's not so horrible," Dr. Grubman said.

ATTACHMENT D

What may get lost in all the merriment is that these are medical procedures with risks, and not all places have a doctor on-site. Rules about who can inject vary from state to state; New York allows physician assistants and registered nurses to do so.

Grant Stevens, the president of the American Society of Aesthetic Plastic Surgery, said he is less concerned about Botox than fillers. Complications can include a Spock eyebrow or a dropped lid from injecting the wrong muscle, but the effects are temporary.

Still, he notes that living with facial asymmetry even for a few months can interfere with one's work and quality of life.

Joey Zauzig takes a selfie after a chemical peel at Ject. Jackie Molloy for The New York Times

Fillers, however, can be injected into the wrong place — between blood vessels, for example — resulting in complications that can include blindness. "It's not as rare as we would all like to think," said Dr. Stevens, who admits to thinking about it every time he gets fillers.

He doesn't think it's necessary to have a doctor inject. ("Heresy!" he said, cheerfully.) But he suggests asking, at the very least, if your beauty bar of choice has a "crash cart," which includes vials of a "doggone expensive" enzyme called hyaluronidase that can reverse an inadvertent

ATTACHMENT D

intravascular injection of hyaluronic acid fillers like Restylane and Juvéderm. Fillers like Radiesse, which are made of other substances, are not reversible, he said.

“Give it all the cute names you want, but it’s not a hair salon,” Dr. Stevens said of the new breed of beauty bars. “It’s the practice of medicine.”

Ject 138 West 10th Street, 917-573-6806; jectnyc.com

Alchemy 43 40 East 21st Street, 917-970-3743; alchemy43.com

Plump 224 West 18th Street, 646-330-7464; plumplife.com

A version of this article appears in print on May 1, 2019, on Page D3 of the New York edition with the headline: I’ll Have Botox And a Filler, Too, Please

ATTACHMENT D

ASDSA
American Society for Dermatologic Surgery ASSOCIATION

Position on the Definition of the Practice of Medicine

The practice of medicine involves diagnosis, treatment, or correction of human conditions, ailments, diseases, injuries, or infirmities whether physical or mental, by any means, methods, devices, or instruments. The practice of medicine includes, but is not limited to:

a. Undertaking to perform any surgical operation upon any person; and

b. Performing any act or procedure that uses a biologic or synthetic material, or chemical application of any kind if it alters or damages or is capable of altering or damaging living tissue; and

c. Performing any act or procedure using a mechanical device, or displaced energy form of any kind if it damages or is capable of damaging living tissue.

Such acts or procedures include, for example, the use of all lasers, light sources, microwave energy, electrical impulses, chemical application, particle sanding, the injection or insertion of foreign or natural substances, cryoablation or soft tissue augmentation. Living tissue is any layer below the dead cell layer (stratum corneum) of the epidermis. The epidermis, below the stratum corneum, and dermis are living tissue layers. Certain FDA-approved Class I and II devices, by their intended or improper use, can damage below the stratum corneum. Therefore, their use and the diagnosis and treatment surrounding their use, constitutes the practice of medicine.

Approved by the ASDSA Board of Directors: October 2015
Reaffirmed October 2019
Reaffirmed March 2023

ATTACHMENT D

American Society for Dermatologic Surgery ASSOCIATION

Position on Delegation

Support

- On-site physician supervision of all non-physicians performing medical procedures including those for cosmetic indications.
- Quality care by ensuring adequately trained non-physicians.
- Clear and transparent communication with the patient about who will be providing care.

Oppose

- Independent practice of non-physicians outside of a physician-led team.
- Physicians overseeing procedures outside of their scope of practice and for which they have no training and/or expertise.

The guiding principle for all dermatologic surgeons is to practice ethical medicine with the highest possible standards. Physicians should be properly trained in all procedures performed to ensure the highest level of patient care and safety. A physician should be fully qualified by residency training and fellowship or appropriate post-graduate training. Training should include an extensive understanding of cutaneous medicine and surgery, the indications for each procedure, and the pre- and post-operative care involved in treatment. Physicians should only claim subspecialization for treatments, conditions, or procedures within the scope of the residency or fellowship training which the physician completed, as described above. The physician may use terms in plain-English – or in languages spoken by patients – to describe the physician's subspecialty so long as the description includes treatments, conditions or procedures within the residency training.

Under the appropriate circumstances, a physician may delegate certain procedures to non-physicians. Ideally, a physician should make the initial assessment of a patient. The supervising physician shall be physically present on-site, immediately available, and able to respond promptly to any question or problems that may occur while the procedure is being performed. It is the responsible physician's obligation to ensure that a non-physician possesses knowledge of cutaneous medicine, documented training in the procedure, the indications for the procedure, and the pre- and post-operative care involved.

Non-physicians, namely physician assistants (PAs) and Nurse Practitioners (NPs), are being implemented in medical settings to improve patient access to care. Historically, non-physicians were introduced as a solution to the growing need for primary care services, especially in underserved areas. As such, there is a lack of formal education and specialty training. The clinical training of these non-physicians includes approximately 500-900[1] hours that spans across a number of medical specialties, of which only a small percentage is cutaneous medicine and surgery, compared to the nearly 10,000 hours of specialized training in the structure, function, and treatment of skin that dermatologists receive in their 3-year residency. In a study of dermatologists using non-physicians in their practice, only 10% of respondents said their PAs or NPs had received formal dermatology training, and just over half had completed a dermatology rotation during their education.[2]

---

[1] Jalian, H.R., C.A. Jalian, and M.M. Avram. *Increased risk of litigation associated with laser surgery by nonphysician operators*. JAMA Dermatol, 2014. **150**(4): p. 407-11.

[2] Hibler B, Rossi A. *The Use of Non-physicians in Cosmetic Dermatology: Legal and Regulatory Standards*. Current Dermatology Reports, **2015**: p. 1-8

ATTACHMENT D

Patients are often confused about who is performing their medical procedures. The alphabet soup of letters after a practitioner's name is confusing for patients who lack familiarity with their degrees and exact level of training they represent. In an American Medical Association survey of patients, 39% of respondents thought that a doctor of nursing was a physician[3]. The use of clear terminology and transparency lessens the likelihood of misunderstandings. ASDSA supports public policy which requires staff directly interacting with patients to wear photo identification listing the individual's name and level of licensure using clear, complete terminology rather than hard to understand acronyms or abbreviations. Likewise, medical advertisements should list the name of persons performing treatments as well as one's level of licensure in similarly clear and complete terminology.

Approved by the ASDSA Board of Directors: December 2015
Updated October 2019
Updated August 2020
Updated October 2024

Additional References:

Kimball, A.B. and J.S. Resneck, Jr., *The US dermatology workforce: a specialty remains in shortage.* J Am Acad Dermatol, 2008. **59**(5): p. 741-5.

Choudhry, S., et al., *State medical board regulation of minimally invasive cosmetic procedures.* J Am Acad Dermatol, 2012. **66**(1): p. 86-91.

Moshell, A.N., P.D. Parikh, and W.J. Oetgen, *Characteristics of medical professional liability claims against dermatologists: data from 2704 closed claims in a voluntary registry.* J Am Acad Dermatol, 2012. **66**(1): p. 78-85.

Brody, H.J., R.G. Geronemus, and P.K. Farris, *Beauty versus medicine: the nonphysician practice of dermatologic surgery.* Dermatol Surg, 2003. **29**(4): p. 319-24.

Friedman, P.M., et al., *Nonphysician practice of dermatologic surgery: the Texas perspective.* Dermatol Surg, 2004. **30**(6): p. 857-63.

Jalian, H.R., C.A. Jalian, and M.M. Avram, *Common causes of injury and legal action in laser surgery.* JAMA Dermatol, 2013. **149**(2): p. 188-93.

---

[3] Global Strategy Group conducted a telephone survey of 850 adults nationwide on behalf of the AMA Scope of Practice Partnership, Aug. 13–18, 2008. The overall margin of error is +/- 3.4 percent at the 95 percent confidence level. Baselice & Associates conducted a follow-up telephone survey of 850 adults nationwide on behalf of the Scope of Practice Partnership, Nov. 4–8, 2010. The overall margin of error is +/- 3.4 percent at the 95 percent confidence level. Baselice & Associates conducted an internet survey of 801 adults on behalf of the AMA Scope of Practice Partnership between May 1–June 6, 2014. The overall margin of error is +/- 3.5 percent at the 95 percent confidence level. Baselice & Associates conducted an internet survey of 802 adults on behalf of the AMA Scope of Practice Partnership, July 12-19, 2018. The overall margin of error is +/- 3.5 percent at the 95 percent confidence level. –for more information visit: https://www.ama-assn.org/system/files/2020-10/truth-in-advertising-campaign-booklet.pdf

[4] Be aware that each state / territory has its own set of laws and regulations that determine the delegation standards one must adhere to.

ATTACHMENT D

Relevant AMA Policy:

H-160.949 Practicing Medicine by Non-Physicians

Our AMA: (1) urges all people, including physicians and patients, to consider the consequences of any health care plan that places any patient care at risk by substitution of a non-physician in the diagnosis, treatment, education, direction and medical procedures where clear-cut documentation of assured quality has not been carried out, and where such alters the traditional pattern of practice in which the physician directs and supervises the care given;

(2) continues to work with constituent societies to educate the public regarding the differences in the scopes of practice and education of physicians and non-physician health care workers;

(3) continues to actively oppose legislation allowing non-physician groups to engage in the practice of medicine without physician (MD, DO) training or appropriate physician (MD, DO) supervision;

(4) continues to encourage state medical societies to oppose state legislation allowing non-physician groups to engage in the practice of medicine without physician (MD, DO) training or appropriate physician (MD, DO) supervision;

(5) through legislative and regulatory efforts, vigorously support and advocate for the requirement of appropriate physician supervision of non-physician clinical staff in all areas of medicine; and

(6) opposes special licensing pathways for “assistant physicians” (i.e., those who are not currently enrolled in an Accreditation Council for Graduate Medical Education training program, or have not completed at least one year of accredited graduate medical education in the U.S).(Res. 317, I-94; Modified by Res. 501, A-97; Appended: Res. 321, I-98; Reaffirmation A-99; Appended: Res. 240, Reaffirmed: Res. 708 and Reaffirmation A-00; Reaffirmed: CME Rep. 1, I-00; Reaffirmed: CMS Rep. 6, A-10; Reaffirmed: Res. 208, I-10; Reaffirmed: Res. 224, A-11; Reaffirmed: BOT Rep. 9, I-11; Reaffirmed: Res. 107, A-14; Appended: Res. 324, A-14; Modified: CME Rep. 2, A-21)

H-160.950 Guidelines for Integrated Practice of Physician and Nurse Practitioner

Our AMA endorses the following guidelines and recommends that these guidelines be considered and quoted only in their entirety when referenced in any discussion of the roles and responsibilities of nurse practitioners: (1) The physician is responsible for the supervision of nurse practitioners and other advanced practice nurses in all settings.

(2) The physician is responsible for managing the health care of patients in all practice settings.

(3) Health care services delivered in an integrated practice must be within the scope of each practitioner's professional license, as defined by state law.

(4) In an integrated practice with a nurse practitioner, the physician is responsible for supervising and coordinating care and, with the appropriate input of the nurse practitioner, ensuring the quality of health care provided to patients.

(5) The extent of involvement by the nurse practitioner in initial assessment, and implementation of treatment will depend on the complexity and acuity of the patients' condition, as determined by the supervising/collaborating physician.

(6) The role of the nurse practitioner in the delivery of care in an integrated practice should be defined through mutually agreed upon written practice protocols, job descriptions, and written contracts.

(7) These practice protocols should delineate the appropriate involvement of the two professionals in the care of patients, based on the complexity and acuity of the patients' condition.

(8) At least one physician in the integrated practice must be immediately available at all times for supervision and consultation when needed by the nurse practitioner.

(9) Patients are to be made clearly aware at all times whether they are being cared for by a physician or a nurse practitioner.

(10) In an integrated practice, there should be a professional and courteous relationship between physician and nurse practitioner, with mutual acknowledgment of, and respect for each other's contributions to patient care.

(11) Physicians and nurse practitioners should review and document, on a regular basis, the care of all patients with whom the nurse practitioner is involved. Physicians and nurse practitioners must work closely enough together to become fully conversant with each other's practice patterns.(CMS Rep. 15 - I-94; BOT Rep. 6, A-95; Reaffirmed: Res. 240, A-00; Reaffirmation A-00; Reaffirmed: BOT Rep. 28, A-09; Reaffirmed: BOT Rep. 9, I-11; Reaffirmed: Joint CME-CMS Rep., I-12; Reaffirmed: BOT Rep. 16, A-13; Reaffirmed: BOT Rep. 09, A-23)

H-475.986 Surgical Assistants other than Licensed Physicians

Our AMA: (1) affirms that only licensed physicians with appropriate education, training, experience and demonstrated current competence should perform surgical procedures;

(2) recognizes that the responsible surgeon may delegate the performance of part of a given operation to surgical assistants, provided the surgeon is an active participant throughout the essential part of the operation. Given the nature of the surgical assistant’s role and the potential of risk to the public, it is appropriate to ensure that qualified personnel accomplish this function;

(3) policy related to surgical assistants states: (a) The surgical assistant is limited to performing specific functions as defined in the medical staff bylaws, rules and regulations. These generally include the following tasks: aid in maintaining adequate exposure in the operating field, cutting suture materials, clamping and ligating bleeding vessels, and, in selected instances, actually performing designated parts of a procedure. (b) It is the surgeon’s responsibility to designate the individual most appropriate for this purpose within the bylaws of the medical staff. The first assistant to the surgeon during a surgical operation should be a credentialed health care professional, preferably a physician, who is capable of participating in the operation, actively assisting the surgeon. (c) Practice privileges of individuals acting as surgical assistants should be based upon verified credentials and the supervising physician’s capability and competence to supervise such an assistant. Such privileges should be reviewed and approved by the institution’s medical staff credentialing committee and should be within the defined limits of state law. Specifically, surgical assistants must make formal application to the institution’s medical staff to function as a surgical assistant under a surgeon’s supervision. During the credentialing and privileging of surgical assistants, the medical staff will review and make decisions on the individual’s qualifications, experience, credentials, licensure, liability coverage and current competence. (d) If a complex surgical procedure requires that the assistant have the skills of a surgeon, the surgical assistant must be a licensed surgeon fully qualified in the specialty area. If a complication requires the skills of a specialty surgeon, or the surgical first assistant is expected to take over the surgery, the surgical first assistant must be a licensed surgeon fully qualified in the specialty area.(e) Ideally, the first assistant to the surgeon at the operating table should be a qualified surgeon or resident in an education program that is accredited by the Accreditation Council for Graduate Medical Education (ACGME) and/or the American Osteopathic Association (AOA). Other appropriately credentialed physicians who are experienced in assisting the responsible surgeon may participate when a trained surgeon or a resident in an accredited program is not available. The AMA recognizes that attainment of this ideal in all surgical care settings may not be practicable. In some circumstances it is necessary to utilize appropriately trained and credentialed unlicensed physicians and non-physicians to serve as first assistants to qualified surgeons.(BOT Rep. 32, A-99; Reaffirmed: Res. 240, 708, and Reaffirmation A-00; Reaffirmed: CMS Rep. 6, A-10; Reaffirmed: BOT Rep. 16, A-13; Modified: BOT Rep. 09, A-23)

ATTACHMENT D

Position on Physician Oversight in Medical Spas

Support:

- Medical decisions that are based on patient outcomes and quality of care
- Appropriate supervision, oversight and training by qualified onsite physicians

Oppose:

- Decision-making based on financial gain
- Large corporately-owned medical spas hiring so-called “medical directors” to supervise “in name only”
- The practice of renting one’s name and medical license in exchange for a fee or percentage of profits
- Inadequate penalties that do not deter physicians from providing deficient supervision

In the interest of patient care and safety, ASDSA opposes in-name-only medical directors without appropriate onsite supervision, oversight and training by qualified[1] physicians.

The problem lies not with the medical spa model, itself, but rather with non-physician-owned medical spas that do not provide adequate physician supervision and oversight. There are many legitimate, safe, physician-owned medical spas that operate with a high standard of patient care. However, lack of regulation and enforcement has enabled a large number of medspas to offer cosmetic medical procedures by inadequately trained or supervised persons to an unsuspecting public.[2] It is estimated by the American Med Spa Association, which states that ideally a doctor should always be on-site, that half of the medical spas operating across the country are not in compliance with the law.[3, 4]

Our Association has, on an ongoing basis, received a number of reports from our members who have been solicited to act as medical directors in name only, in a medical spa, or “medspa” in exchange for a fee. We have become increasingly concerned about the proliferation of non-physicians practicing medicine and its impact on patient safety. Recent studies conducted by the ASDSA have shown an increase in patient complications resulting from this trend. A 2013 study of laser complications by non-physicians published in Journal of the American Medical Association (JAMA) found that, from 1999-2012, a total of 64% (n=48) of cases related to injury from cutaneous laser surgery performed by a non-physician arose in a

---

[1] Qualified is defined in ASDSA’s *Position Statement on Chemical Peels.* https://www.asds.net/Portals/0/PDF/asdsa/asdsa-position-statement-chemical-peels.pdf “Physicians should be properly trained in all procedures performed to ensure the highest level of patient care and safety. They should be qualified by residency training that includes an extensive understanding of cutaneous medicine and surgery, the indications for each procedure and the pre- and post-operative care involved in treatment.

[2] Hogan S, Wood E, Mishra V. Who Is Holding the Syringe? A Survey of Truth in Advertising Among Medical Spas [published online ahead of print, 2023 Sep 26]. Dermatol Surg. 2023;10.1097/DSS.0000000000003929.

[3] O’Brien, P. *The Texas Med Spa IV Therapy Death: What You Need to Know.* American Med Spa Association. https://americanmedspa.org/blog/the-texas-med-spa-iv-therapy-death-what-you-need-to-know

[4] In 2020 the American Med Spa Association changed their position regarding direct on-site supervision of non-physician providers but in 2023 they continue to highlight the need for proper supervision and delegation when administering medical procedures in medical spas. https://americanmedspa.org/blog/the-texas-med-spa-iv-therapy-death-what-you-need-to-know

nonmedical practice setting. Between 2008 and 2011, the same study found that procedures performed in medical spas by non-physicians account for almost 80% of lawsuits.[5]

Financial incentives for performing medical procedures in a medical spa setting are inherent to the business model, which more closely represents a retail store than a medical practice. Incentives for non-physician providers to maximize revenue generation in a spa can increase the risk of adverse events. Additionally, non-physician providers who are rewarded for performing increasingly more laser services, without proper physician oversight, may also encourage the treatment of patients who are not suitable candidates for laser treatments. This environment may lead to non-physician providers valuing business goals over patient safety.[6]

A California law passed in 2012 provides an excellent model with regard to appropriate penalties for violation of the corporate practice of medicine ban in medical spa facilities.[7] The law provides that when a business organization either employs a California physician, or contracts with him/her to serve as a "medical director" of a health care practice he/she does not own, and the business organization provides medical care that ordinarily can only be provided by the holder of a valid California medical license – actions already prohibited by California law -- that conduct will be subject to penalties that are more proportionate to the risks to which patients are exposed, and more proportionate to the money of which they're being defrauded.

Before stricter penalties were passed, medspa chains created business management and franchising schemes that violated the law. The too-common practice of lay-owned businesses hiring so-called medical directors was already prohibited but poorly enforced. Prior to the passage of this law, Joint Medical Board/Nursing Board hearings in 2007 concluded better enforcement was needed of existing California law that prohibits laypersons or corporate entities from owning any part of a medical practice.

Approved by the ASDSA Board of Directors: October 2015
Reaffirmed December 2019
Updated January 2024

---

[5] JAMA Dermatol. 2014; 150(4):407-411. doi: 10.1001/jamadermatol.2013.7117

[6] Alam, M; Dover, J.S; Arndt, K.A. Use of Cutaneous Lasers and Light Sources: Appropriate Training and Delegation. *Skin Therapy Letter*. 2007; 12, 5: 5-9

[7] AB-1548 Practice of medicine: cosmetic surgery: employment of physicians and surgeons. Retrieved from: http://leginfo.legislature.ca.gov/faces/billTextClient.xhtml;jsessionid=355e2701012f9f9b2b82f015e282?bill_id=201120120AB1548

[9] Gibson J, Greif C, Nijhawan RI. Evaluating Public Perceptions of Cosmetic Procedures in the Medical Spa and Physician's Office Settings: A Large-scale Survey. Dermatol Surg. 2023;10.1097/DSS.0000000000003811.

[10] ASDSA's *Medical Spa Safety Act Model Legislation*. https://www.asds.net/Portals/0/PDF/asdsa/asdsa-medical-spa-safety-act.pdf

ATTACHMENT D

Related AMA Policy:

D-35.983 Addressing Safety and Regulation in Medical Spas

Our AMA will: (1) advocate for state regulation to ensure that cosmetic **medical** procedures, whether performed in **medical spas** or in more traditional **medical** settings, have the same safeguards as "medically necessary" procedures, including those which require appropriate training, supervision and oversight; (2) advocate that cosmetic **medical** procedures, such as botulinum toxin injections, dermal filler injections, and laser and intense pulsed light procedures, be considered the practice of medicine; (3) take steps to increase the public awareness about the dangers of those **medical spas** which do not adhere to patient safety standards by encouraging the creation of formal complaint procedures and accountability measures in order to increase transparency; and (4) continue to evaluate the evolving issues related to **medical spas**, in conjunction with interested state and **medical** specialty societies.

ATTACHMENT D

Position on the Regulation of Physician Assistants

Support:

- Maintaining the authority of medical licensing and regulatory boards to regulate medicine through oversight of physicians, physician assistants and related medical personnel.

Oppose:

- The establishment of autonomous physician assistant regulatory boards outside of the medical board authority and purview.

In the interest of protecting patient safety, the authority to license, regulate and discipline physician assistants should be under the jurisdiction of existing state medical licensing and regulatory boards. Originally created in the mid 1960's[1] to support physicians and help alleviate primary care shortages, the physician assistant profession was designed to function under the direction and supervision of a duly qualified licensed physician. American Medical Association (AMA) policy states that the extent of the involvement of a physician assistant in the assessment and implementation of treatment should be determined by the supervising physician.[2] AMA policy also states that a physician assistant should provide patient care only in accordance with the state's medical practice act and other state law, and such law should provide that the physician assistant's utilization be approved by the medical licensing board.[3] ASDSA believes that in order to ensure patient safety and quality care, the practice of medicine[4] should only be performed by licensed physicians and their properly trained and qualified delegates under the direct, on-site supervision of a licensed physician.[5] As physicians are licensed, regulated and disciplined by state medical licensing and regulatory bodies and are ultimately responsible for the scope of the physician assistant's duties, physician assistant licensure, regulation and disciplinary action should be under the jurisdiction of the state medical licensing board. Currently, the majority of states authorize the medical licensing boards to license, regulate and discipline physician assistants.[6]

Approved by the ASDSA Board of Directors: May 2017
Updated January 2020
Reaffirmed March 2024

---

[1] History of the Profession - Physician Assistant Program | Boston University. (n.d.). Retrieved March 07, 2017, from https://www.bu.edu/paprogram/pa-profession/history-of-the-profession/

[2] AMA Policy Finder*: Physician Assistants and Nurse Practitioners* H-160.947 – 2013 https://policysearch.ama-assn.org/policyfinder/detail/h-160.947?uri=%2FAMADoc%2FHOD.xml-0-761.xml

[3] AMA Policy Finder: *Physician Assistants* H-35.989 - 2011 https://policysearch.ama-assn.org/policyfinder/detail/H-35.989?uri=%2FAMADoc%2FHOD.xml-0-2996.xml

[4] ASDSA *Position Statement on the Definition of the Practice of Medicine* – https://www.asds.net/Portals/0/PDF/asdsa/asdsa-position-statement-definition-of-the-practice-of-medicine.pdf

[5] ASDSA *Position Statement on Delegation* – https://www.asds.net/Portals/0/PDF/asdsa/asdsa-position-statement-delegation.pdf

[6] FSMB. (2016). U.S. Medical Regulatory Trends and Actions. Retrieved March 7, 2017, from https://www.fsmb.org/Media/Default/PDF/FSMB/Publications/us_medical_regulatory_trends_actions.pdf

ATTACHMENT D

Related AMA Policy:

H-160.947 Physician Assistants and Nurse Practitioners

Our AMA will develop a plan to assist the state and local medical societies in identifying and lobbying against laws that allow advanced practice nurses to provide medical care without the supervision of a physician

The suggested Guidelines for Physician/Physician Assistant Practice are adopted to read as follows (these guidelines shall be used in their entirety):

(1) The physician is responsible for managing the health care of patients in all settings.

(2) Health care services delivered by physicians and physician assistants must be within the scope of each practitioner's authorized practice, as defined by state law.

(3) The physician is ultimately responsible for coordinating and managing the care of patients and, with the appropriate input of the physician assistant, ensuring the quality of health care provided to patients.

(4) The physician is responsible for the supervision of the physician assistant in all settings.

(5) The role of the physician assistant in the delivery of care should be defined through mutually agreed upon guidelines that are developed by the physician and the physician assistant and based on the physician's delegatory style.

(6) The physician must be available for consultation with the physician assistant at all times, either in person or through telecommunication systems or other means.

(7) The extent of the involvement by the physician assistant in the assessment and implementation of treatment will depend on the complexity and acuity of the patient's condition and the training, experience, and preparation of the physician assistant, as adjudged by the physician.

(8) Patients should be made clearly aware at all times whether they are being cared for by a physician or a physician assistant.

(9) The physician and physician assistant together should review all delegated patient services on a regular basis, as well as the mutually agreed upon guidelines for practice.

(10) The physician is responsible for clarifying and familiarizing the physician assistant with his/her supervising methods and style of delegating patient care.

(BOT Rep. 6, A-95; Reaffirmed: Res 240 and Reaffirmation A-00; Reaffirmed: Res. 213, A-02; Modified: CLRPD Rep. 1, A-03; Reaffirmed: BOT Rep. 9, I-11; Reaffirmed: Joint CME-CMS Rep., I-12; Reaffirmed: BOT Rep. 16, A-13; Reaffirmed: Res. 206, I-22; Reaffirmed: CMS Rep. 09, A-23)

H-35.989 Physician Assistants

ATTACHMENT D

1. Our AMA opposes legislation to increase public funding for programs to train physician assistants and supports a careful reevaluation of the need for public funding at the time that present legislative authorities expire.

2. A physician assistant should provide patient care services only in accord with the medical practice act and other applicable state law, and such law should provide that the physician assistant's utilization by a physician or group of physicians be approved by the medical licensing board. A licensed physician or group of physicians seeking to utilize a physician assistant should submit to the medical licensing board an application for utilization that identifies: the qualifications and experience of the physician assistant, the qualifications and experience of the supervising physician and a description of his or her practice, and a description of the manner and the health care settings in which the assistant will be utilized, and the arrangements for supervision by the responsible physician. Such an application should also specify the number of physician assistants that the physician or group of physicians plans to employ and supervise. A physician assistant should be authorized to provide patient care services only so long as the assistant is functioning under the direction and supervision of a physician or group of physicians whose application for utilization has been approved by the medical licensing board. State medical licensing boards, in their review of applications for utilization of a physician assistant, should take special care to insure that the proposed physician assistant functions not be of a type which: (a) would unreasonably expand the professional scope of practice of the supervising physician, (b) cannot be performed safely and effectively by the physician assistant, or (c) would authorize the unlicensed practice of medicine.

3. The physician assistant should function under the direction of and supervision by a duly qualified licensed physician. The physician must always maintain the ultimate responsibility to assure that high quality care is provided to every patient. In discharging that responsibility, the physician should exercise that amount of control or supervision over a physician assistant which is appropriate for the maintenance of quality medical care and in accord with existing state law and the rules and regulations of the medical licensing authority. Such supervision in most settings includes the personal presence or participation of the physician. In certain instances, such as remote practice settings, where the physician assistant may function apart from the supervising physician, such remote function (if permitted by state law) should be approved by the state medical licensing board on an individual basis. Such approval should include requirements for regular reporting to the supervising physician, frequent site visits by that physician, and arrangements for immediate communication with the supervising physician for consultation at all times. The physician assistant may serve the patients of the supervising physician in all types of health care settings, including but not limited to: physician's office, ambulatory or outpatient facility, clinic, hospital, patient's home, long-term care facility or nursing home. The state medical licensing board should determine on an individual basis the number of physician assistants that a particular physician may supervise or a group of physicians may employ.

4. While it is preferable and desirable that the physician assistant be employed by a physician or group of physicians so as to ensure appropriate physician supervision in the interests of the patient, where a physician assistant is employed by a hospital, the physician assistant must provide patient care services in accordance with the rules and procedures established by the organized medical staff for utilization of physician-employed physician assistants functioning in that institution, and under the direction and supervision of a designated physician who has been approved by the state medical licensing board to supervise that physician assistant in accordance with a specific utilization plan and who shall be directly responsible as the attending physician for the patient care services delegated to his physician assistant.

5. The AMA opposes legislation or proposed regulations authorizing physician assistants to make independent medical judgments as to the drug of choice for an individual patient.

6. In view of an announced interest by HHS in considering national legislation which would override state regulatory systems for health manpower, the AMA recommends that present Association policy supporting state prerogatives in this area be strongly reaffirmed.

7. Our AMA opposes legislation or regulation that allows physician assistant independent practice.

(BOT/CME/CMS Joint Rep., I-80; Reaffirmed: CLRPD Rep. B, I-90; Reaffirmation A-99; Reaffirmed: CME Rep. 2, A-09; Reaffirmed: BOT Rep. 9, I-11; Appended: Res. 230, I-17; Reaffirmed: BOT Rep. 12, A-23; Reaffirmed: Res. 208, I-23)

D-35.985 Support for Physician Led, Team Based Care

Our AMA:

1. Reaffirms, will proactively advance at the federal and state level, and will encourage state and national medical specialty societies to promote policies H-35.970, H-35.973, H-35.974, H-35.988, H-35.989, H-35.992, H-35.993, H-160.919, H-160.929, H-160.947, H-160.949, H-160.950, H-360.987, H 405.969 and D-35.988.

2. Will identify and review available data to analyze the effects on patients? access to care in the opt-out states (states whose governor has opted out of the federal Medicare physician supervision requirements for anesthesia services) to determine whether there has been any increased access to care in those states.

3. Will identify and review available data to analyze the type and complexity of care provided by all non-physician providers, including CRNAs in the opt-out states (states whose governor has opted out of the federal Medicare physician supervision requirements for anesthesia services), compared to the type and complexity of care provided by physicians and/or the anesthesia care team.

4. Will advocate to policymakers, insurers and other groups, as appropriate, that they should consider the available data to best determine how non-physicians can serve as a complement to address the nation's primary care workforce needs.

5. Will continue to recognize non-physician providers as valuable components of the physician-led health care team.

6. Will continue to advocate that physicians are best qualified by their education and training to lead the health care team.

7. Will call upon the Robert Wood Johnson Foundation to publicly announce that the report entitled, "Common Ground: An Agreement between Nurse and Physician Leaders on Interprofessional Collaboration for the Future of Patient Care" was premature; was not released officially; was not signed; and was not adopted by the participants.

ATTACHMENT D

(BOT Rep. 9, I-11; Reaffirmed: CMS Rep. 1, A-12; Reaffirmed: CMS Rep. 07, A-17; Reaffirmed: CMS Rep. 10, A-19; Reaffirmed: CMS Rep. 6, A-21)

ATTACHMENT D

Spa | Health + Wellness

Australia's First Filler Blindness Case Serves as a Cautionary Tale

Tatiana Bido , Special Projects Editor | August 22, 2018

ATTACHMENT D

brought to the ophthalmology department at Prince of Wales Hospital in Sydney, but doctors were not able to restore sight in her right eye. Prince of Wales Hospital opthamologist and medical retina speciali Dr. John Downie says although it's rare, the risk of blindness is possible because of the blood vessels around the eye and nose are in continuity with blood vessels around the retina. "The filler or the other substance is inadvertently injected into one of the blood vessels in the skin or under the skin around the eye and that material goes back along that artery to one of the bigger arteries behind the eye and then can flow and then block of the blood vessels going to the eye or inside the eye."

You May Also Like: Plastic Surgeons Warn That this Popular Cosmetic Procedure Can Cause Blindness

According to *Four Corner*'s report, across the world, 98 people have reportedly gone blind from injectec filler. The patient in Australia was said to have had her filler procedure performed by a nurse practitione at a beauty salon, without a doctor present, which is not an unusual practice these days. It's this growin trend of having injectable treatments done outside of a qualified doctor's office that has many physician worried about exacerbated risks and complications that can occur when choosing an unqualified injecto

For Largo, FL oculoplastic surgeon Jasmine Mohadjer, MD, the danger of fillers causing blindness is not new, but she says it is a risk that is rare and minimized when a patient does their homework. "I think tha any time you do a procedure like this, even though it's considered noninvasive, a patient should take it seriously and find a reputable place and provider. Whoever does the procedure needs to be qualified, trained, certified and well-versed in the anatomy of the area and potential complications and be ready t recognize the complication in a timely manner."

"Blindness is an exceedingly rare complication when using filler," explains Dr. Mohadjer, "but there are certain areas that are more high risk than others. If filler gets inside of a blood vessel and shoots off like an embolus, it essentially acts like a small stroke to that area. Blood is not getting to the eye because th filler is occluding the blood vessel. You want an injector that is not only knows where to inject and what to inject—for instance, I would never inject filler in the glabellar area where Botox is often used—but also techniques to avoid complications such as this."

The takeaway from the *Four Corners* investigation is the same message Dr. Mohadjer preaches,

ATTACHMENT D

0 COMMENTS ▼

Tags: Cosmetic Treatments • Health + Wellness • Jasmine Mohadjer, Md • News • Spa • Blindness • Dermal Fillers • Injectables And Fillers • Side Effects

Related Stories

ATTACHMENT D

ATTACHMENT D

ADULT ACNE

This Common Acne Medication Almost Made One Woman Go Blind

"When I was admitted to the hospital, they told me I was a day way from being completely blind."

READ ARTICLE→

ATTACHMENT D

NEWS

After 3 Women Are Blinded, This Controversial Procedure Is Back in the Spotlight

What to know about any alternative treatments.

READ ARTICLE→

ATTACHMENT D

The 6 Best Volume-Boosting Products Made for Fine Hair

5 Secrets to Aging in Reverse

How to Stop Your Eyes From Aging You

The 6 Most High-Tech Facials to Try in Miami

EXPERT LOGIN

USERNAME

PASSWORD

NewBeauty may earn a portion of sales from products that are purchased through our site as part of our affiliate partnerships with retailers.

ATTACHMENT D

Global Headquarters
101 Park Avenue
4th Floor
New York, NY 10178

Corporate Headquarters
3651 NW 8th Ave.
Boca Raton. FL 33431
info@sandow.com

Received: 11 June 2020 | Revised: 13 July 2020 | Accepted: 24 July 2020

ATTACHMENT D

DOI: 10.1111/jocd.13645

COSMETIC COMMENTARY

JCD Journal of Cosmetic Dermatology

WILEY

Differentiation in a market of imitation: The evolving world of aesthetic dermatology

Jordan V. Wang MD, MBE, MBA[1,2] | Nazanin Saedi MD[1] | Roy G. Geronemus MD[2]

[1]Department of Dermatology and Cutaneous Biology, Thomas Jefferson University, Philadelphia, Pennsylvania

[2]Laser & Skin Surgery Center of New York, New York, New York

Correspondence
Jordan V Wang, MD, MBE, MBA, Laser & Skin Surgery Center of New York, 317 E 34th Street, 6th Floor Research Department, New York, NY 10016.
Email: drjordanwang@gmail.com

Abstract

This commentary examines the recent general movement in the field of cosmetic dermatology toward imitation and reproduction. The issues of medical spas, nonphysician operators, and counterfeit products have recently garnered interest in aesthetic dermatology. As physicians, it is our professional and bioethical responsibility to ensure that our patients are educated on the presence of medical spas, nonphysician operators, and counterfeit products in our field, especially given the discrepancies in patient safety and outcomes. There are also actions that dermatologists can take in order to help differentiate themselves in this current market. This will not only protect our field, but also our patients, who we are obligated to provide high-quality care for as physicians.

KEYWORDS

aesthetics, dermatology, lasers, marketing, patient safety

1 | INTRODUCTION

Over the past few decades, the field of aesthetic dermatology has continued to evolve. What was once considered a small subspecialty has now transformed into an independently flourishing field of its own. The popularity of cosmetic procedures has considerably increased, especially as minimally invasive procedures have captured the attention of patients. In such a rapidly expanding and highly profitable aesthetic market, dilemmas will inevitably develop. More recently, increased attention has focused on a general movement in our field toward imitation and reproduction. Aesthetic dermatologists should be aware of these current trends and strategies to help differentiate themselves as providers.

2 | MEDICAL SPAS

Medical spas have recently proliferated. In the most populous cities, they have even outnumbered cosmetic dermatologists and plastic surgeons.[1] Consumer interest has largely been fueled by persuasive marketing campaigns with particular emphasis on social media outreach. Unfortunately, the growth of medical spas has outpaced cosmetic dermatologists, which has likely been accelerated by disparate state regulations covering their oversight. Of all cosmetic complications encountered by members of the American Society for Dermatologic Surgery (ASDS) in the past 2 years, the majority reported that 61%-100% were attributable to medical spas.[2] These were believed to be the result of improper training and education, technique, and device settings. When examining litigation cases associated with nonphysician operators performing laser surgery from 2008 to 2011, nearly 80% of lawsuits originated from medical spas.[3] Some states are laxer than others (eg, allowing nurses or naturopaths to be medical directors, nonphysician operators to practice without physician supervision, and medical directors to be off-site), and there is relatively limited enforcement. Until the patchwork of state regulations are either more strictly reformed or unified, the proliferation of medical spas will likely continue.

Patients should be educated on the discrepancies in safety and outcomes between practice settings. Physicians can help to

differentiate themselves by openly advertising their expertise, and the dermatology clinic should promote itself as a physician-based practice. For example, all professional degrees and certifications should be visible in high-traffic areas, and any apparel, such as scrubs, should include professional credentials. The projected image of the physician should be consistent across all media platforms and outreach materials in order to convey a consistent message to patients.

3 | NONPHYSICIAN OPERATORS

Attempts to expand access to dermatologic care has led to an increase in physician extenders and technicians, who often perform cosmetic procedures.[4] Although they can work under the supervision of dermatologists, they have recently transitioned to settings where sufficient oversight can be an afterthought, such as salons, spas, shopping centers, personal homes, psychiatry offices, and dentistry offices. Even physicians who are not trained for aesthetic procedures and/or are from other specialties that are nonrelated to dermatology are playing an active role. In medical spas, physician extenders and aestheticians were the treating practitioner for 76% of locations, while medical directors were not even on-site for over half of the businesses.[5] These medical directors were often nonphysicians themselves, including nurses and physician assistants. Over the years, it has been argued that nonphysician operators lack the required expertise of physicians that comes from years of training and have a much higher turnover rate leading to additional training concerns of the replacement staff.

Cosmetic dermatology lends itself to many nuances that must be mastered—ideally through a formal certified training program, such as the ASDS-accredited Cosmetic Dermatologic Surgery Fellowship. Sufficient instruction can decrease adverse events and improve patient safety, especially in a field that has been exploited by less experienced providers practicing cookbook medicine. Aesthetic physicians should spread public awareness on the benefits of being treated by credentialed practitioners. They can also advertise their affiliations with academic institutions and memberships in professional societies, such as the ASDS. Societies have pushed for truth in advertising campaigns and clear communication of credentials, which is supported by the ASDS's model legislation for the Medical Spa Safety Act.[6]

4 | COUNTERFEIT PRODUCTS

The appearance of counterfeit products in aesthetics has garnered recent attention. In a 2019 survey, about 40% of aesthetic practitioners admitted to encountering them.[7] In terms of safety, 20.1% and 39.7% had encountered patients with adverse events from counterfeit medical devices and injectables, respectively. Nearly 1 in 20 practitioners purchased a counterfeit medical device, which doubled to 1 in 10 for injectables. Although often much cheaper, these products have not been formally tested using certified quality control measures and, therefore, offer no assurances of safety and efficacy to the practitioner and patient. Unfortunately, patients are unlikely to know when they are being treated with counterfeit products.

Aesthetic physicians should hold themselves to a higher standard and consider patient safety above other factors, including financial profits. They should only procure products from authorized retailers to avoid the inadvertent purchase of counterfeits, which was the case for nearly 80% of those who had bought counterfeit injectables.[7] Physicians should also be aware that secondary markets can sell devices from reputable brands, but these may not have received regular maintenance and/or may be ineligible for future service by the manufacturer. Physicians should warn patients when treatment with counterfeits is suspected by other practitioners. Additionally, they can directly show authentic products to patients, including packaging and labeling, prior to any procedure. This can help to train patients to request practitioners to do so in the future and can serve as an additional opportunity for patient education.

5 | CONCLUSIONS

In the ever-evolving world of aesthetics, consumers regularly fall victim to those who develop the best marketing strategies. Unfortunately, dermatologists are often unprepared and the least adept to fight this battle.[8] However, the real power of cosmetic physicians is in their education and training. They should ensure that their image and brand are appropriately portrayed to consumers to reflect this. This is the true voice of being a physician in the aesthetic field, and it should not be taken lightly. It is our professional and bioethical responsibility to ensure that patients are educated on the impact of medical spas, nonphysician operators, and counterfeit products in our field, especially given the stark differences in patient safety and outcomes. Although recent studies have begun to examine some of their dangers, additional studies are still needed in order to comprehensively evaluate their impact to our field and determine effective strategies to mitigate their risks. This will not only protect our field, but also our patients, who we are obligated to provide high-quality care for as physicians.

CONFLICT OF INTEREST

The authors have no relevant conflicts of interest to declare.

ORCID

Jordan V. Wang https://orcid.org/0000-0001-7437-2745

REFERENCES

1. Wang JV, Albornoz CA, Noell C, Friedman PM, Zachary CB, Saedi N. Skewed distribution of medical spas and aesthetic physician

practices: A cross-sectional market analysis. *Dermatol Surg*. 2020. [Epub ahead of print].
2. Wang JV, Albornoz CA, Goldbach H, et al. Experiences with medical spas and associated complications. *Dermatol Surg*. 2020. [Epub ahead of print].
3. Jalian HR, Jalian CA, Avram MM. Increased risk of litigation associated with laser surgery by nonphysician operators. *JAMA Dermatol*. 2014;150(4):407-411.
4. Resneck JS Jr, Kimball AB. Who else is providing care in dermatology practices? Trends in the use of nonphysician clinicians. *J Am Acad Dermatol*. 2008;58(2):211-216.
5. Wang JV, Shah S, Albornoz CA, Rohrer T, Zachary CB, Saedi N. Medical spa or physician practice: The national impact of patient wait times in aesthetics. *Dermatol Surg*. 2020. [Epub ahead of print].
6. American Society for Dermatologic Surgery. Model Legislation-Medical Spa Safety Act. <https://www.asds.net/Portals/0/PDF/asdsa/asdsa-medical-spa-safety-act.pdf>. Accessed 22 March 2020.
7. Wang JV, Hattier G, Rohrer T, Zachary CB, Saedi N. experiences with counterfeit aesthetic medical devices and injectables. *Dermatol Surg*. 2019. [Epub ahead of print].
8. Wang JV, Albornoz CA, Hazan E, Keller M, Saedi N. Business administration training for dermatology residents: Preparing for the business of medicine. *Clin Dermatol*. 2019;37(1):78-79.

How to cite this article: Wang JV, Saedi N, Geronemus RG. Differentiation in a market of imitation: The evolving world of aesthetic dermatology. *J Cosmet Dermatol*. 2020;00:1–3. https://doi.org/10.1111/jocd.13645

Evolution of Search Trends for Medical Spas and Cosmetic Dermatologists: A 2009 to 2019 National Comparison

Over the past decade, the popularity of cosmetic procedures has continued to rise. A recent member survey of the American Society for Dermatologic Surgery (ASDS) found that in 2018, more than 3.7 million injectable procedures were performed.[1] Compared with the previous 7 years, soft tissue filler treatments increased by 78%; body contouring procedures rose by about 400%; and laser, light, and energy-based treatments grew by 74%. As the demand for minimally and noninvasive cosmetic procedures continues to surge, medical spas have capitalized on this by proliferating across the country. As of 2018, there were over 5,400 medical spas posting an average revenue of more than $1.5 million. These aesthetic facilities offer treatments similar to those performed in physician-based practices, often with discounted prices and shorter wait times. It is possible that these facilities could also be viewed as less intimidating than traditional medical offices and may even be more accessible to consumers in certain areas, especially rural locations. However, compared with physician practices, medical spas have been associated with deficiencies in training, improper technique, and incorrect device settings.[2] There is also evidence to suggest an increased risk of medical professional liability claims for laser surgery performed by nonphysicians.[3] Despite the contrast in practice environment, consumers continue to line up at these well-marketed facilities.

Patient's interest in medical subjects can be measured by various means. One such method to track overall consumer interest is through the evaluation of online search engine queries. Various studies have demonstrated how patients consult and rely on information on the Internet when researching medical topics and searching for practitioners, especially in the field of cosmetics. A recent study identified Google Search as the most popular source and third most trusted source from which to obtain information about cosmetic treatments.[4] Therefore, the use of online search engine data can serve as a proxy for measuring consumer interest.

To assess consumer interest in medical spas and cosmetic dermatologists, we examined the available data for search terms from the Google search engine through its proprietary Google Trends platform on February 13, 2020. We queried all search requests in the United States from January 2009 through December 2019. The particular keywords of interest were "medical spa" and "cosmetic dermatologist." The term "dermatologist" was not used because the term was too broad, and we wanted to narrow results to only include cosmetic practitioners in the field to allow for accurate comparison with medical spas. Other variations did not yield enough search data. These data were analyzed and further examined by geographic area. Interest over time is a value that Google defines as the number relative to the highest value for a given region and time. Peak popularity for a term is represented by a value of 100, whereas any other number is in proportion to that. When there is not enough data available for a set time point or region, a value of 0 is assigned by default.

From January 2009 to December 2019, the interest for "medical spa" was greater than that of "cosmetic dermatologist" ($p < .00001$) (Figure 1). This was true for all monthly time points during this period. The interest for medical spa peaked in April 2011, which is also when there was the greatest difference in popularity between the 2. Compared with all other seasons, spring had the greatest interest for both medical spa

ISSN: 1076-0512 • Dermatol Surg 2020;00:1–3 •

ATTACHMENT D

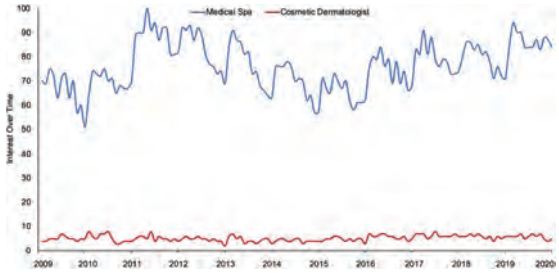


Figure 1. Search queries from Google for "medical spa" and "cosmetic dermatologist" from 2009 to 2019. Data source: Google Trends (https://www.google.com/trends).

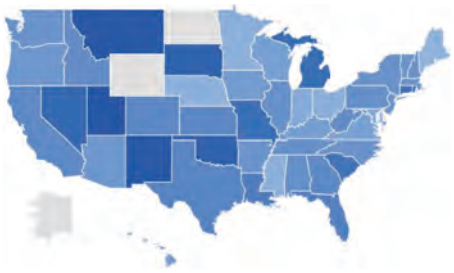


Figure 3. Search queries from Google for "medical spa" in 2009 to 2019 by geographic area. Data source: Google Trends (https://www.google.com/trends).

(p = .0004) and cosmetic dermatologist (p = .0262), whereas the fall had the least interest for both (p = .0002 and p = .0028, respectively). There was a cyclical seasonal pattern. Since 2015, the interest for medical spa seemed to be increasing for all seasons (Figure 2).

For medical spa, the 10 states with the greatest interest were Utah (100), Montana (91), New Mexico (87), Rhode Island (80), South Dakota (79), Oklahoma (77), Nevada (73), Michigan (67), Missouri (62), and Connecticut (59) (Figure 3). For cosmetic dermatologist, the 10 states with the greatest interest were Maryland (100), Florida (98), New York (87), New Jersey (85), California (76), Pennsylvania (72), Massachusetts (68), Illinois (67), Texas (65), and Ohio (58) (Figure 4). It is interesting to note that numerous geographic areas did not have enough data available from searches for cosmetic dermatologist, whereas this occurred with only a few areas for medical spa. There is a stark contrast between Figures 3 and 4.

Overall, the data showed significantly greater consumer interest in medical spas compared with cosmetic dermatologists on a consistent basis over the past 11 years.

Since 2015, the interest in medical spas began to rise, which may correlate with the increase in number of new facilities. It is clear that medical spas—whether through aggressive marketing campaigns, search engine optimization, or their sheer prevalence—have cemented a prominent position within the aesthetic consumer space. Unsurprisingly, medical spas are often owned and/or operated by those with adequate business training, who can more effectively target consumer populations than the average dermatologist. The business education of dermatologists was recently shown to be insufficient and inadequate during residency training.[5]

We also observed an interesting cyclical pattern based on seasonality with both medical spas and cosmetic dermatologists—experiencing peaks in popularity in the spring and nadirs in the fall. This information can help aesthetic physicians. For example, it can help to better optimize marketing strategies and inventory management. In terms of geographic distribution, searches for cosmetic dermatologists were primarily concentrated on the East and West coasts along with Texas. The skewed distribution of cosmetic dermatologists across the country likely plays a role, with a traditional preference for larger metropolitan areas.

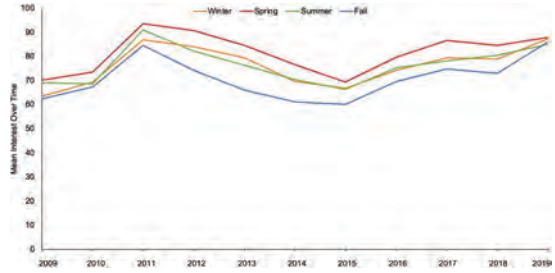


Figure 2. Search queries from Google for "medical spa" by season from 2009 to 2019. Data source: Google Trends (https://www.google.com/trends).

Figure 4. Search queries from Google for "cosmetic dermatologist" in 2009 to 2019 by geographic area. Data source: Google Trends (https://www.google.com/trends).

By contrast, medical spas were popular fairly evenly throughout the country with more interest concentrated in the Midwest. Additional studies should explore how variations in state-specific medical spa regulations affect consumer interest and demand.

This study expands our current knowledge in the aesthetic field by highlighting the consumer interest in medical spas and cosmetic dermatologists over an 11-year period throughout the United States. By extrapolating search engine data from Google, we now have more powerful information on aesthetic consumer patterns. These findings have important clinical implications, especially given the implicated differences in patient safety and outcomes between medical spas and physician-based cosmetic practices.

References

1. American Society for Dermatologic Surgery. *Survey on Dermatologic Procedures: Report of 2018 Procedures*. Available at: https://www.asds.net/portals/0/PDF/procedures-survey-results-presentation-2018.pdf. Accessed February 25, 2020.
2. Wang JV, Albornoz CA, Goldbach H, Mesinkovska N, et al. Experiences with medical spas and associated complications: a survey of aesthetic practitioners. Dermatol Surg 2020. doi:10.1097/DSS.0000000000002344. Epub Ahead of Print.
3. Jalian HR, Jalian CA, Avram MM. Increased risk of litigation associated with laser surgery by nonphysician operators. JAMA Dermatol 2014; 150:407–11.
4. Wang JV, Zachary CB, Saedi N. Factors influencing consumer decisions in aesthetics: selection of procedures and practitioners. Dermatol Surg 2020. doi:10.1097/DSS.0000000000002084. Epub Ahead of Print.
5. Wang JV, Albornoz CA, Hazan E, Keller M, et al. Business administration training for dermatology residents: preparing for the business of medicine. Clin Dermatol 2019;37:78–9.

Jordan V. Wang, MD, MBE, MBA*
Christian A. Albornoz, MD*
Christopher B. Zachary, MBBS, FRCP†
Nazanin Saedi, MD*
**Department of Dermatology and Cutaneous Biology*
Thomas Jefferson University
Philadelphia, Pennsylvania
†Department of Dermatology
University of California
Irvine, California

The authors have indicated no significant interest with commercial supporters.

Experiences With Medical Spas and Associated Complications: A Survey of Aesthetic Practitioners

Jordan V. Wang, MD, MBE, MBA,* Christian A. Albornoz, MD,* Hayley Goldbach, MD,† Natasha Mesinkovska, MD, PhD,† Thomas Rohrer, MD,‡ Christopher B. Zachary, MBBS, FRCP,† and Nazanin Saedi, MD*

BACKGROUND Medical spas have experienced a recent rise in popularity. However, rules and regulations vary nationwide. Given the number of complications attributable to medical spas, questions remain about currently regulatory practices and whether they are sufficient to protect patients from harm.

OBJECTIVE Our study investigated the current state of medical spas and their associated patient complications in the aesthetic field as well as the experiences and attitudes of practitioners.

MATERIALS AND METHODS A survey was distributed to current members of the American Society for Dermatologic Surgery.

RESULTS Of all cosmetic complications encountered in the past 2 years, the majority reported that the percentage of complications seen in their practice attributable to medical spas ranged from 61% to 100%. The most commonly cited complications from medical spas were burn, discoloration, and misplacement of product, whereas the most commonly cited treatments resulting in complications were fillers, intense pulsed light, and laser hair removal. For safety and outcomes, medical spas were rated as inferior to physician-based practices.

CONCLUSION Patient complications associated with medical spas are not uncommon. Overall, practitioners believe medical spas are endangering to patient safety, think that stricter rules and regulations are necessary, and request more support from the specialty medical societies.

The authors have indicated no significant interest with commercial supporters.

In a society which places a growing value on aesthetic beauty, the prevalence of noninvasive and minimally invasive cosmetic procedures has continued to rise. A recent member survey of the American Society for Dermatologic Surgery (ASDS) demonstrated that in 2018, over 3.7 million injectable procedures were performed.[1] Injection of filler products experienced a 78% increase from 2012. Laser, light, and energy-based treatments grew by 74%, and body sculpting procedures increased over 400% during this time period. The increasing popularity of aesthetic treatments has undoubtedly contributed to the trend of medical spas opening across the country.

These aesthetically focused facilities offer treatments similar to those historically performed in physician-based practices—often at discounted prices—but with varying standards of oversight and credentialing. Ironically, the efforts of states to improve access to primary health care by loosening the regulations for nonphysician providers have fostered an appetite for more lucrative aesthetic services in a spa environment. These state legislations have created an influx of nonphysician providers practicing aesthetic services with either no or partial supervision, despite vocal opposition from various specialty societies, such as the ASDS and American Academy of Dermatology.[2,3] Owing to a gross lack of uniform regulations between

*Department of Dermatology and Cutaneous Biology, Thomas Jefferson University, Philadelphia, Pennsylvania; †Department of Dermatology, University of California, Irvine, California; ‡SkinCare Physicians, Chestnut Hill, Massachusetts

ISSN: 1076-0512 • Dermatol Surg 2020;46:1543–1548 • DOI: 10.1097/DSS.0000000000002344

states, the roles and responsibilities of providers have become increasingly blurred, and the divide between aesthetic dermatology and cosmetology has narrowed. The detrimental consequences of this shift are clear and have already resulted in various adverse events for patients and consumers.

Tracking adverse events attributable to nonphysicians or nondermatology providers is difficult. Previous studies have examined complication rates, but this does not paint a complete picture. Although the literature has consistently demonstrated low complication rates with most procedures, these studies have traditionally focused on board-certified dermatologists or plastic surgeons as opposed to other providers who may possess more limited training or skillset.[4] These reports may therefore underrepresent the true rate of adverse events related to cosmetic procedures in all settings and falsely minimize the true potential for harm to patients.

Despite the recent attention focused on the rise of medical spas in aesthetic medicine, no formal studies have thoroughly examined their presence in the field in connection with their associated complications through a national survey of aesthetic practitioners. Our study aims to fill this gap in the literature by surveying members of the ASDS. Our results offer information and insights into how we can better educate practitioners and patients about the potential risks and dangers.

Materials and Methods

Online surveys were distributed via the Internet to current members of the ASDS as of 2019. Each individual was asked for demographic data, as well as their experiences interacting with and attitudes toward medical spas and associated complications.

Results

A total of 306 respondents completed the survey. There was a mean 13.9 years of experience working in aesthetic medicine. The majority worked in an urban setting (56.9%) compared with suburban (40.5%) and rural (2.6%) locations. For the vast majority (80.7%), the closest medical spa was <5 minutes away using typical transportation for the area.

In the past 2 years, the majority (70.3%) of respondents have had 1 to 20 patients experience cosmetic complications from medical spas. Of all cosmetic complications encountered in the past 2 years, the majority (63.1%) reported that the percentage of complications seen in their practice attributable to medical spas ranged from 61% to 100% (Figure 1).

The top 5 most cited cosmetic complications from medical spas were burn (89.7%), discoloration (80.1%), misplacement of product (74.6%), scar (69.4%), and bruise (52.9%) (Figure 2). The top 5

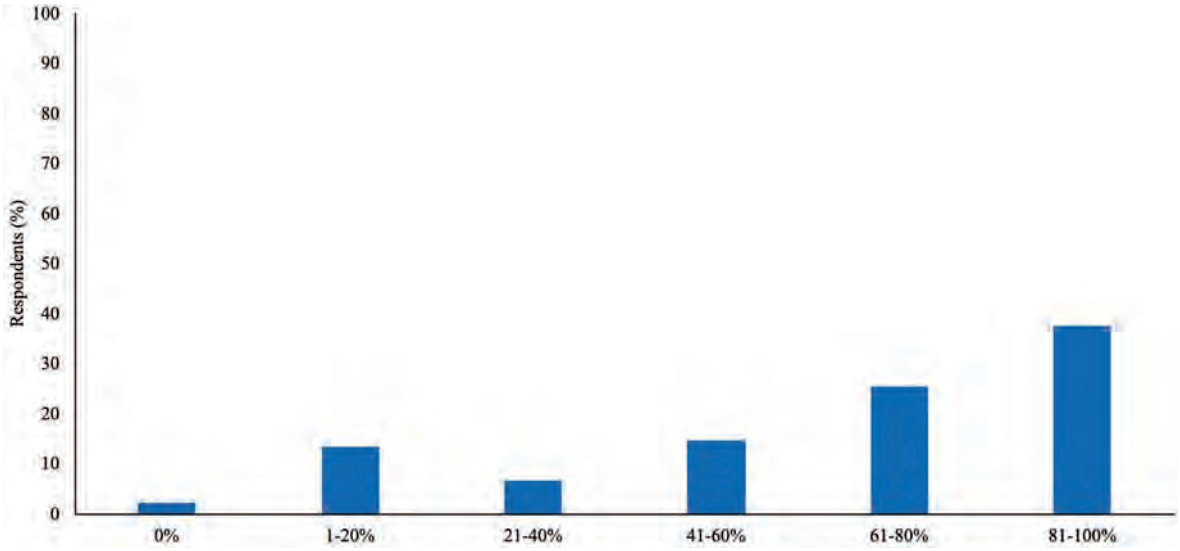


Figure 1. Percentage of all cosmetic complications in the past 2 years which were associated with medical spas.

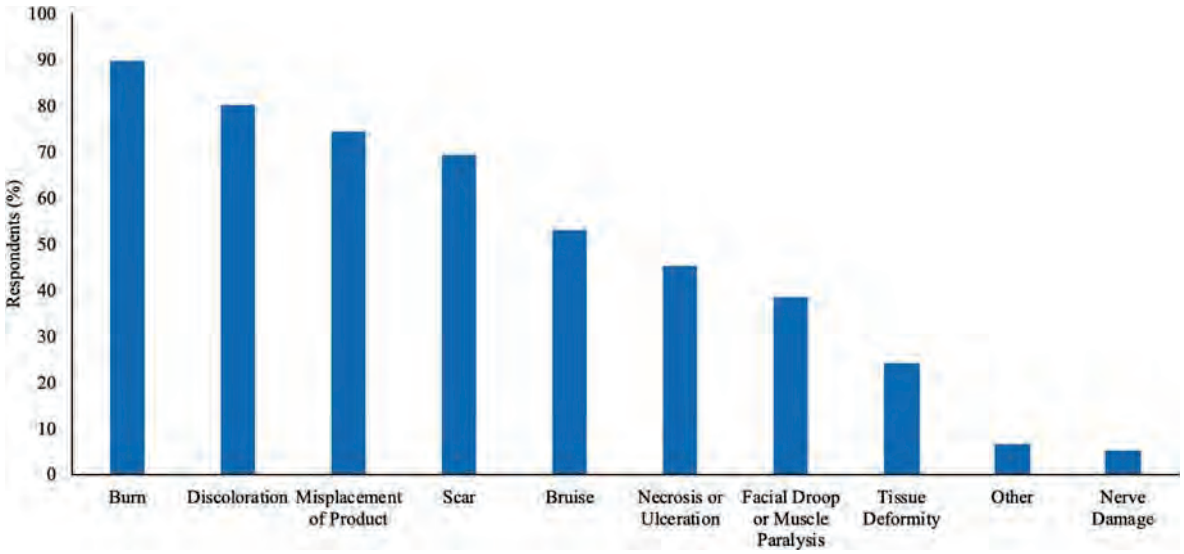


Figure 2. Types of cosmetic complications associated with medical spas.

most cited treatments resulting in complications were fillers (80.4%), intense pulsed light (74.9%), laser hair removal (73.4%), neurotoxins (54.0%), and lasers for discoloration (50.5%) (Figure 3). The top 3 most cited reasons for why these complications may have occurred were improper training or education (90.0%), improper technique (88.3%), and improper device setting (77.3%).

When the training background of the medical director for the medical spa was known, the top 3 most cited specialties were family medicine (40.9%), obstetrics/gynecology (25.1%), and emergency medicine (23.7%). Interestingly, dermatology was the least cited (2.4%) (Figure 4).

Regarding safety, medical spas were rated by respondents to be worse than the average physician practice for fillers (97.6%), intense pulsed light (95.2%), skin tightening and resurfacing (94.3%), laser hair removal (91.3%), laser tattoo removal (89.6%), neurotoxins (80.9%), and body contouring (67.6%).

Regarding outcomes, medical spas were rated by respondents to be worse than the average physician

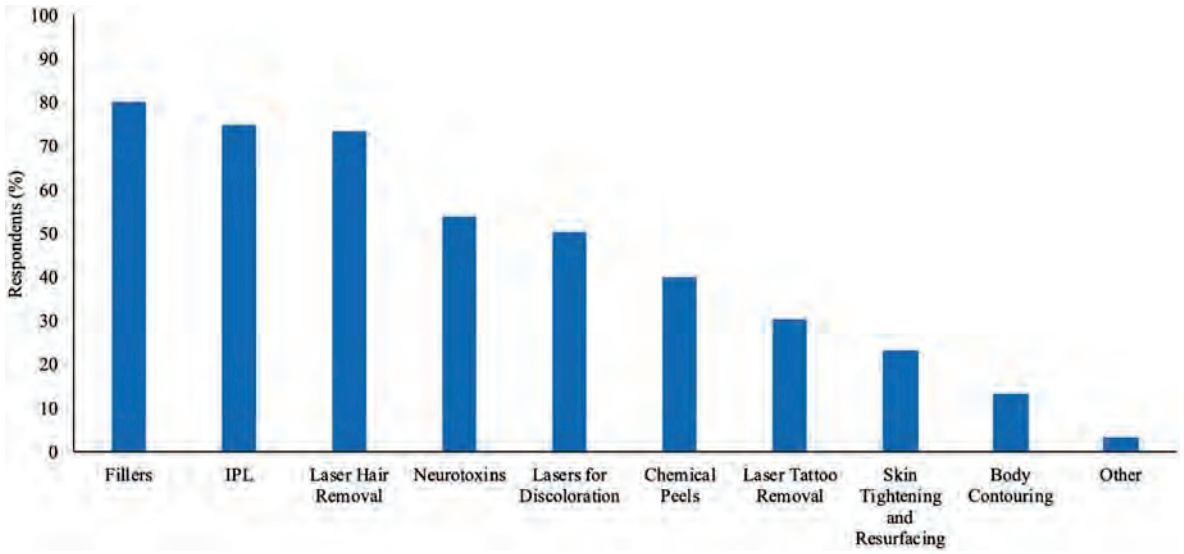


Figure 3. Sources of cosmetic complications associated with medical spas.

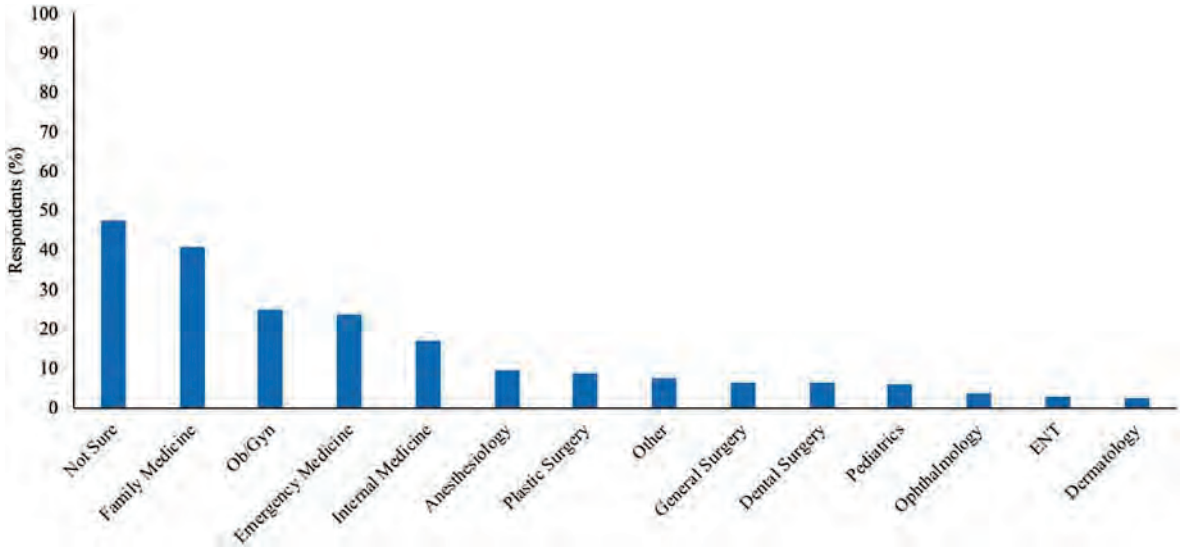


Figure 4. Training background of medical director for medical spa when complications were encountered.

practice for fillers (96.6%), skin tightening and resurfacing (92.0%), intense pulsed light (91.2%), neurotoxins (89.0%), laser tattoo removal (86.0%), laser hair removal (80.2%), and body contouring (69.6%).

The majority (58.8%) believed medical spas are either very or extremely endangering to patient safety. The majority (67.0%) was either not familiar with or only somewhat familiar with the rules and regulations, whereas 95.8% believed these should be stricter. Most respondents (84.3%) would like more information and support from medical societies.

Discussion

Demand for noninvasive and minimally invasive aesthetic procedures continues to grow at a remarkable pace. Medical spas have capitalized on this opportunity with over 5,400 facilities across the country in 2018, representing a total value approaching nearly $10 billion.[5] Many of these facilities are located in states that do not require direct physician oversight and are often managed by nurse practitioners, nurses, and naturopaths. A recent study demonstrated that the majority of medical directors possessed training backgrounds that were neither dermatology nor plastic surgery.[6] Interestingly, nearly 30% of the interviewed medical spas had a medical director who did not perform any procedures themselves, and nearly half were off-site for the majority of the time. Inconsistent supervision and disparate state-by-state regulations coupled with the rapid expansion of medical spas have created a perfect storm for patient endangerment.

The majority of respondents had a medical spa within 5 minutes of their workplace, which is consistent with the recent expansion. An alarming majority also treated several patients who suffered a cosmetic complication from a medical spa. Furthermore, cosmetic complications from medical spas comprise a significant portion of complications treated by responding practitioners. Although this study certainly has recall bias due to the inherent nature of the survey, no other studies have yet to thoroughly examine these trends, and this study begins to shed light on this topic.

The survey attempted to address the systemic faults associated with medical spas that may be responsible for these adverse outcomes. Respondents suspected that the most common reasons for these complications may be improper training, technique, and device settings. However, the causes of complications were likely assumed in many cases. Further investigation into the background of the medical directors also revealed an interesting trend. The top 3 most cited specialties were family medicine, obstetrics/gynecology, and emergency

medicine, whereas dermatology was by far the least cited at 2.4%. Interestingly, plastic surgery was cited at only 8.9%. Furthermore, the field continues to expand, and physicians from other specialties, such as general surgery and pediatrics, have ventured into the procedural aesthetic field.[7]

Expertise certainly plays an integral role in patient safety and outcomes. Very few specialties outside of dermatology and plastic surgery dedicate comparable clinical training to mastering skin pathology, anatomy, and medical and aesthetic treatments. A retrospective biopsy study found that dermatologists were more clinically accurate at diagnosing neoplastic and cystic lesions than nondermatologists, including family physicians, various surgeons, internists, and pediatricians.[8] Compounding these issues, physicians—dermatologists included—are increasingly delegating aesthetic procedures to physician extenders whose qualifications and training lack a universal standard.[9] To further highlight the associated dangers, numerous reports have begun to surface documenting the cosmetic referral of pigmented lesions that are ultimately diagnosed as melanomas.[10]

Regarding the safety and outcomes of common cosmetic procedures, respondents consistently rated medical spas as inferior to the average physician-based practice, especially for laser devices. However, these numbers may be somewhat skewed because practicing dermatologists may have an inherent bias. A recent study demonstrated that laser hair removal was the most commonly litigated procedure, with nonphysicians operating these devices 40% of the time.[11] From 2008 to 2011, the percentage of medical professional liability claims stemming from cutaneous laser surgery performed by nonphysicians increased by nearly 115%, from 36.3% to 77.8%.[12] During the same time period, procedures performed by nonphysicians in medical spas represented almost 80% of lawsuits. Adequate training and proper treatment are vital to patient safety, and sufficient oversight can provide an additional layer of protection.

Nearly two-thirds of respondents reported that they were not familiar with or only somewhat familiar with current guidelines governing medical spas. Unfortunately, rules and regulations are not universal. There are nationwide variations in state medical board bylaws regulating the number of nonphysicians a single physician may supervise, the requirement of physicians to be on-site, and the extent to which delegation of procedural tasks may occur.[13] For these reasons, it is clear why most respondents desired more information and support from our field's medical societies. Additional advocacy on behalf of patients, consumers, and physicians is needed to regulate acceptable standards of care at medical spas across the country.

Conclusion

Patients who have experienced complications from medical spas are not uncommon in aesthetic dermatology. Overall, practitioners believe medical spas are endangering patient safety, think that stricter rules and regulations are necessary, and request more support from the specialty medical societies.

References

1. American Society for Dermatologic Surgery. *2018 ASDS Survey on Dermatologic Procedures*. 2018. Available from: https://www.asds.net/portals/0/PDF/procedures-survey-results-infographic-2018.pdf. Accessed August 15, 2019.
2. American Society for Dermatologic Surgery Association. *Position on Physician Oversight of Medical Spas*. Available from: https://www.asds.net/Portals/0/PDF/asdsa/asdsa-position-statement-physician-oversight-in-medical-spas.pdf. Accessed August 15, 2019.
3. American Academy of Dermatology Association. *Position Statement on Medical Spa Standards of Practice*. Available from: https://www.aad.org/forms/policies/uploads/ps/ps-medical%20spa%20standards%20of%20practice.pdf. Accessed August 15, 2019.
4. Alam M, Kakar R, Nodzenski M, Ibrahim O, et al. Multicenter prospective cohort study of the incidence of adverse events associated with cosmetic dermatologic procedures: lasers, energy devices, and injectable neurotoxins and fillers. JAMA Dermatol 2015;151:271–7.
5. American Med Spa Association. *2019 Medical Spa State of the Industry: Executive Summary*. Available from: https://www.americanmedspa.org/page/med-spa-statistics. Accessed August 15, 2019.
6. Gibson JF, Srivastava D, Nijhawan RI. Medical oversight and scope of practice of medical spas (med-spas). Dermatol Surg 2019;45:581–7.
7. Housman TS, Hancox JG, Mir MR, Camacho F, et al. What specialties perform the most common outpatient cosmetic procedures in the United States? Dermatol Surg 2008;34:1–7.

8. Sellheyer K, Bergfeld WF. A retrospective biopsy study of the clinical diagnostic accuracy of common skin diseases by different specialties compared with dermatology. J Am Acad Dermatol 2005; 52:823–30.

9. Resneck JS Jr, Kimball AB. Who else is providing care in dermatology practices? Trends in the use of nonphysician clinicians. J Am Acad Dermatol 2008;58:211–6.

10. Stankiewicz K, Chuang G, Avram M. Lentigines, laser, and melanoma: a case series and discussion. Lasers Surg Med 2012;44: 112–6.

11. Jalian HR, Jalian CA, Avram MM. Common causes of injury and legal action in laser surgery. JAMA Dermatol 2013;149:188–93.

12. Jalian HR, Jalian CA, Avram MM. Increased risk of litigation associated with laser surgery by nonphysician operators. JAMA Dermatol 2014;150:407–11.

13. Choudhry S, Kim NA, Gillum J, Ambavaram S, et al. State medical board regulation of minimally invasive cosmetic procedures. J Am Acad Dermatol 2012;66:86–91.

Address correspondence and reprint requests to: Jordan V. Wang, MD, MBE, MBA, Department of Dermatology and Cutaneous Biology, Thomas Jefferson University, 833 Chestnut Street, Suite 740, Philadelphia, PA 19107, or e-mail: jordan.wang@jefferson.edu

ATTACHMENT D

General and Plastic Surgery Advisory Committee Panel Meeting on Soft-tissue Fillers

Mathew Avram, MD, JD, President

American Society for Dermatologic Surgery Association (ASDSA)

ASDSA
American Society for Dermatologic Surgery ASSOCIATION

- Fillers are seeing increased patient demand: the 2019 ASDS Procedures Survey showed dermatologic surgeons administered 1.6 million soft-tissue filler injections, up 78% over eight years.

- ASDS convened a multidisciplinary Soft Tissue Fillers Evidence-based Guideline Task Force:
  - 8 board certified dermatologists (ASDSA members)
  - 1 plastic surgeon
  - 1 facial plastic and reconstructive surgeon
  - 1 oculoplastic surgeon
  - 2 patient representatives
  - 1 methodologist
- The ASDS-led Fillers Guideline TF determined that the topic of preventing and treating adverse events of injectable fillers required the development of evidence-based clinical practice guidelines to support decision-making in daily practice.

- Knowledge of vascular anatomy is essential for all filler injectors (Board certified dermatologists/physcians have this education)
- **Intravascular injection is possible at any injection location on the face, but certain locations carry a higher risk.**
- Accidental injection of filler into facial arteries can cause:
  - filler embolization and vascular occlusion, leading to tissue ischemia
  - necrosis
  - visual abnormalities
  - blindness
  - stroke

- Filler adverse events are likely underreported and increasing in frequency as the popularity of injectable fillers grows
- Physician offices are likeliest to report errors
- ASDSA/Northwestern University developed the Cutaneous Procedures Adverse Events Reporting (CAPER) system.
  - Voluntary reporting of adverse events during dermatologic surgery procedures.
  - Data used to help monitor; identify practice and/or education gaps.
  - Identify any potential risk factors for adverse events.
  - More information at *www.caper.net*.

The TF addressed the eight following strategies to reduce injection-related visual compromise:

1. **Obtain informed consent from the patient regarding the rare possibility of IRVC, which can have life-altering consequences.**
2. Develop and post an IVRC protocol, review it with team members, and always have ample hyaluronidase on hand.
3. Stop injecting at first sign of visual compromise, which usually occurs during or immediately after injection and is most often unilateral. Half of the patients show skin involvement, ophthalmoplegia, or ptosis, of which most resolve. Headache, nausea, and vomiting may or may not be present.

ATTACHMENT D

4. Conduct evaluation of immediate post event visual status BEFORE any intervention. **The importance of this cannot be overstated.**
5. Document visual acuity in each eye separately and note in chart.
6. Keep patient informed of evolving events, notify family member, and accompany both through entire process.

Original Article

Preventing and Treating Adverse Events of Injectable Fillers: Evidence-Based Recommendations From the American Society for Dermatologic Surgery Multidisciplinary Task Force

Derek H. Jones, MD,* Rebecca Fitzgerald, MD,† Sue Ellen Cox, MD,† Kimberly Butterwick, MD,‡ V. Hassan Murad, MD,‖ Shannon Humphrey, MD,¶ Jean Carruthers, MD,** Steven H. Dayan, MD,†† Lisa Donofrio, MD,‡‡ Nowell Solish, MD,§§ G. Jackie Yee, MD,‖‖ and Murad Alam, MD¶¶

All injectable fillers may be associated with common injection site reactions such as redness, swelling, bruising, and tenderness, which usually resolve within 1 to 2 weeks. Rare but more serious adverse events from injectable fillers include vascular occlusion leading to skin necrosis or blindness, inflammatory events, and nodule formation, among others.[1] Although rare, they are likely underreported and increasing in frequency as the popularity of injectable fillers grows. Such adverse events can be distressing to both patient and physician and present therapeutic and potential legal challenges.[2] The American Society for Dermatologic Surgery (ASDS) has determined that the topic of preventing and treating these adverse events of injectable fillers requires the development of evidence-based clinical practice guidelines to support decision-making in daily practice.

Methods

American Society for Dermatologic Surgery convened a multidisciplinary task force that consisted of ASDS member physician specialists (8 board-certified in dermatology, 2 in plastic and reconstructive surgery, and 1 in oculoplastic surgery), 2 patient representatives, and a methodologist. The committee task force identified a priori 6 critical questions and commissioned the Mayo Clinic Evidence-based Practice Center to conduct systematic reviews to summarize the relevant evidence. These reviews are published separately.[3] The committee used the GRADE approach (Grading of Recommendations, Assessment, Development and Evaluation), which rates the certainty of evidence as high, moderate, low, or very low. Randomized trials start with a high certainty rating that can be lowered based on various factors and observational studies start with a low certainty rating that can be lowered or raised based on various factors.[4] The GRADE approach leads to 2 types of recommendations: (1) strong recommendations (most compelling, to be applied in most situations with minimal variation) that are denoted by the term "recommend," and (2) conditional recommendations (variation in care is acceptable based on the context and patient's values) that are denoted by the term "suggest." The determination of the strength of recommendation is based on the certainty of evidence, balance of benefits and harms, patient's values, resources, acceptability, and feasibility.[5]

Prevention of Vascular Occlusion, Blindness, and Stroke

Background

Accidental injection of filler into facial arteries can cause filler embolization and vascular occlusion, leading to tissue ischemia, necrosis, visual abnormalities, blindness, and stroke. Knowledge of vascular anatomy is essential for all filler injectors. Intravascular injection is possible at any injection location on the face, but certain locations carry a higher risk.

Recommendations

Although there is no absolutely risk-free injection protocol, ASDS Task Force recommends the following strategies to reduce the risk of vascular occlusion with injectable fillers (Strong recommendation, Moderate certainty evidence):

From the *Skin Care and Laser Physicians of Beverly Hills, Los Angeles, California; †Private Practice, Los Angeles, California; ‡Aesthetic Solutions, Assoc Clinical Faculty, UNC Department of Dermatology, Consulting Association, Duke University Department Dermatology, Chapel Hill, North Carolina; §Cosmetic Laser Dermatology, San Diego, California; ‖Evidence-based Practice Center, Mayo Clinic, Rochester, Minnesota; ¶Department of Dermatology and Skin Sciences, University of British Columbia, Vancouver, Canada; **Department of Ophthalmology and Visual Sciences, University of British Columbia, Vancouver, Canada; ††Plexus Research, Clinical Assistant Professor, University of Illinois, Chicago, Illinois; ‡‡Department of Dermatology, Yale University School of Medicine, New Haven, Connecticut; §§Department of Dermatology, University of Toronto, Toronto, Canada; ‖‖Duke Plastic Surgery, Miami, Florida; ¶¶Departments of Dermatology, Otolaryngology, and Surgery, Northwestern University, Chicago, Illinois

D. H. Jones is an investigator or consultant for Allergan, Galderma, Merz and Revance. R. Fitzgerald is a Consultant for Allergan, Galderma, and Revance, and a Trainer for Galderma. S. E. Cox is investigator and/or Consultant for Allergan, Cosmo, Evolus, Galderma, Merz and Revance. K. Butterwick is an Investigator or Consultant for Allergan, Galderma, Merz, Sciton, Sunevia, Histogen, Revance, and Evolus. M. H. Murad is a publication methodologist with partial funding from ASDS to perform this work. S. Humphrey is a Consultant/Investigator/Speaker for Allergan, Galderma, and Revance, a Consultant/Speaker for Merz, and L'Oreal, a Consultant for Sinclair Pharma, and an Investigator for Evolus. J. Carruthers is a Consultant and Investigator with Allergan, Alphaeon, Bioxis, and Revance, and receives Royalties from Elsevier and UpToDate. S. Dayan is an Investigator or Consultant for Allergan, Galderma, Merz and Revance. L. Donofrio is a Consultant or Investigator for Carefully Scientific, Galderma, Allergan, and Revance. N. Solish is an Investigator or Consultant for Allergan, Galderma, Merz, Cosmo, and Revance. G.J. Yee is a Consultant for Allergan, Galderma, Revance, and Endo Aesthetics. The remaining author has indicated no significant interest with commercial supporters.

Address correspondence and reprint requests to: Derek H. Jones, MD, Skin Care and Laser Physicians of Beverly Hills, 9201 W. Sunset Boulevard, Suite 602, Los Angeles, CA 90069, or e-mail: derekjonesmd@gmail.com

http://dx.doi.org/10.1097/DSS.0000000000002921

ASDSA
American Society for Dermatologic Surgery ASSOCIATION

DERMATOLOGIC SURGERY

7. In patients with signs or symptoms (s/s) of central nervous system (CNS) involvement, contact your local hospital's emergency stroke service and call 911 for immediate transport to the emergency room. In the absence of s/s, evaluate and image the patient to rule out CNS involvement once the ocular event has been addressed. *Time is of the essence. Immediately contact an eye expert who is familiar with this risk and its management. A preexisting relationship with an oculoplastic surgeon, ophthalmologist, and/or retina specialist can avoid unnecessary delays.*

8. Hyaluronidase injections are quick, safe, and easily done at the bedside, and should be considered immediately. Inject .150 units hyaluronidase into the treated area, all areas of skin ischemia, and along the path of arteries leading to the eye. Similar doses can be injected adjacent to and in the supraorbital and supratrochlear foramina. Repeat in quick succession as needed. Retrobulbar (RBH) and peribulbar (PBH) injections may be beneficial, but this remains controversial at this time. {Keep detailed notes of events, interventions, and timing, and all interactions with patient, family, specialists, and facilities. Inform the product manufacturer of the incident for FDA reporting.}

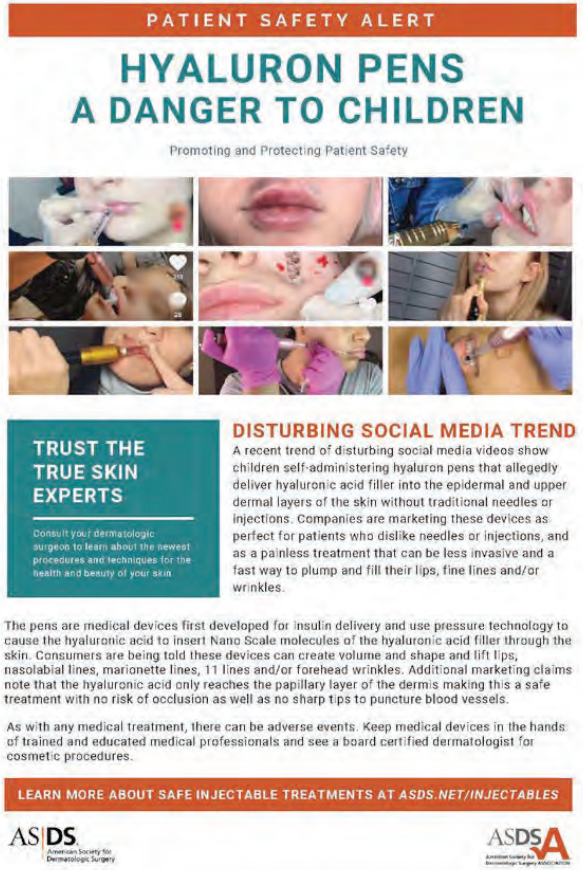
COVID-19 Vaccines & Fillers

- ASDS reviewed FDA safety data from the Moderna vaccine trial
- Three participants out of 15,184 patients who received at least one dose of mRNA-1273 developed facial or lip swelling presumed to be related to dermal filler placement.
- All events resolved after treatment
- Physcians most likely to report complications

ATTACHMENT D

ASDSA Alert: Hyaluron Pens Danger

- ASDSA reported to the FDA the disturbing trend regarding children/public buying and using "hyaluron pens" to inject hyaluronic acid filler into the epidermal and upper dermal layers of the skin.
- Board certified dermatologists have seen social media where children use these pens to self-inject and promote their use to peers.



ASDSA pledges its help to the FDA in making sure fillers are safely given to patients and stay in the hands of physicians who can properly supervise other medical personnel

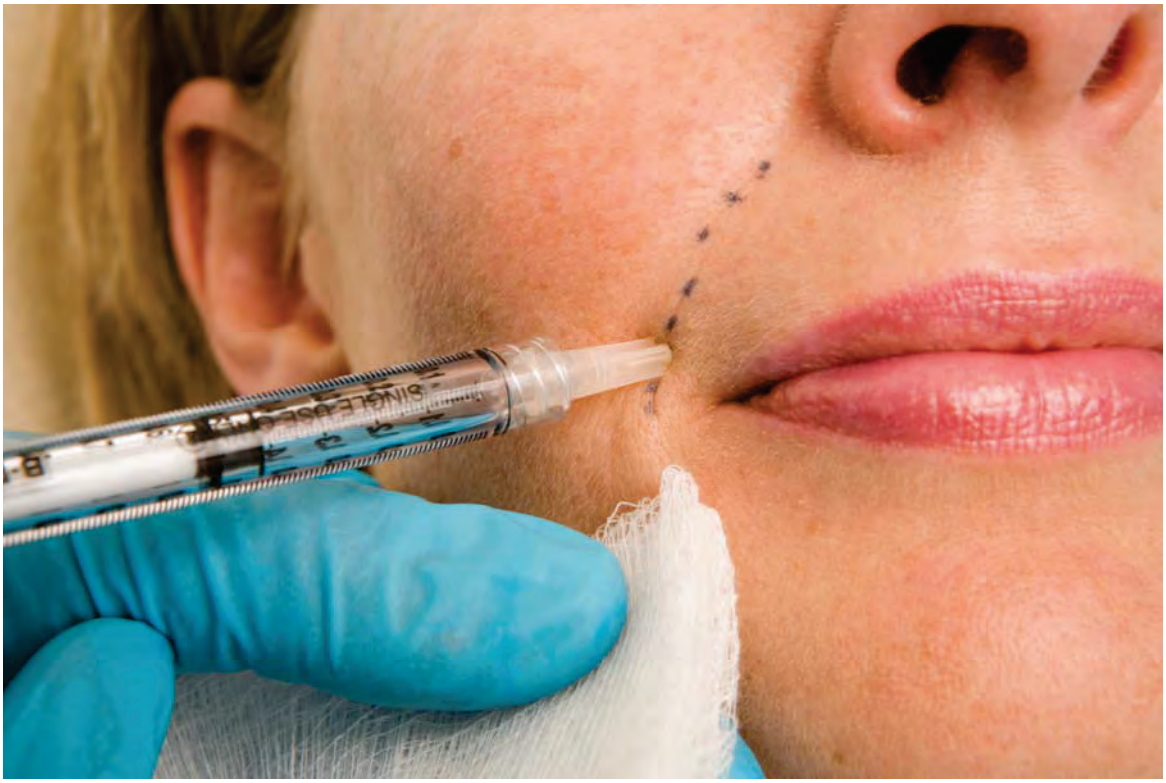
We respectfully ask the FDA consider renaming this panel: "General, Plastic and **Dermatologic** Surgery Advisory Committee" to reflect board certified dermatologists' contributions and expertise in these areas

Thank you

Questions can be directed to *advocacy@asds.net*

ATTACHMENT D

Filling in Wrinkles Safely



Being injected with dermal fillers poses some risks. The most common side effects include: bruising, redness, swelling, pain, and itching. Additional side effects include: infections, lumps and bumps, and discoloration or change in pigmentation.

Español (/consumers/articulos-en-espanol/como-rellenar-las-arrugas-de-una-manera-segura)

These days, people across the country are seeking treatments to smooth smile lines and crow's feet and to plump up their lips and cheeks.

One treatment involves injecting dermal fillers into the face. In studies of dermal fillers approved by the U.S. Food and Drug Administration, people generally report they are satisfied with their treatment results.

ATTACHMENT D

But injectable dermal fillers are not for everyone and may not be indicated for people with certain conditions (such as bleeding disorders or certain allergies). If your health care provider confirms that dermal fillers are an option for you, know that all products have benefits and risks. The FDA advises you to work with a licensed health care provider and to understand all of the risks and benefits *before* receiving treatment. (See more safety tips below.)

What are dermal fillers, and how are they used?

In general, injectable dermal fillers are intended to help fill in wrinkles and give a smoother appearance. They are generally injected into the skin with a needle and are regulated by the FDA as medical devices.

Temporary fillers include the following materials:

- Collagen injections, made of highly purified cow or human collagen
- Hyaluronic acid gel, a protective lubricating gel, produced naturally by the body
- Calcium hydroxylapatite, a mineral and a major component of bone
- Poly-L-lactic acid (PLLA), a biodegradable, biocompatible, synthetic material

These products are used for correcting soft tissue defects in the face, such as moderate to severe facial wrinkles and skin folds, lip and cheek augmentation, and to restore or correct the signs of facial fat loss in people with human immunodeficiency virus (HIV). An FDA approved dermal filler is also used to fill in the back of the hand.

Most FDA-approved fillers are temporary and achieve a smoothing or “filling” effect, which lasts for about six months or longer in most people. (These injectable dermal fillers are temporary because the body eventually absorbs them.)

That said, not all products have been approved for every indication. You can find specific information on each product by reading the FDA’s list of approved dermal fillers (/dermal-fillers-approved-center-devices-and-radiological-health).

The FDA has approved only one permanent wrinkle filler, which contains “polymethylmethacrylate” beads. These are tiny round, smooth, biocompatible plastic particles that are not absorbed by the body. The filler is FDA-approved only for correcting facial tissue around the mouth.

ATTACHMENT D

Although the FDA has approved certain injectable dermal fillers for use in the face (for example, to enhance lips and cheeks) and the hands, the FDA has never approved any injectable fillers for large-scale body contouring or enhancement.

That means you should never get an injectable filler intended as a breast filler, "butt filler," or muscle filler. And you should never get any type of injectable filler for any other large-scale body contouring or body enhancement.

Dermal fillers are not FDA approved for large-scale body contouring and can lead to serious injury, permanent scarring or disfigurement, and even death. (Read "The FDA Warns Against Injectable Silicone for Body Contouring and Enhancement" (/consumers/consumer-updates/fda-warns-against-injectable-silicone-body-contouring-and-enhancement) to learn more.)

What are the risks of FDA-approved fillers?

Remember to work with a licensed health care provider to ask what you can expect for FDA-approved fillers. Then contact your health care provider if you are concerned about a particular side effect.

The most common side effects include:

- bruising
- redness
- swelling
- pain
- itching

Additional side effects less commonly reported include:

- infections
- lumps and bumps
- discoloration or change in pigmentation

Rare but serious risks include:

- scarring, blurred vision, partial vision loss, and blindness if the dermal filler is inadvertently injected into a blood vessel. It is recommended that health care

ATTACHMENT D

providers take care to avoid injection into blood vessels (especially around the forehead, nose and eye area) for these reasons.

- allergic reaction that may lead to a severe reaction (anaphylactic shock) that requires emergency medical help.

Most side effects occur shortly after injection and go away within two weeks. In some cases, side effects may emerge weeks, months, or years later. Talk to your licensed health care provider if you have questions or concerns.

5 Tips for Consumers About Injectable Dermal Fillers

1. **ALWAYS** work with a licensed health care provider who uses properly labeled, sealed vials for treatments. You also can ask to confirm that you are receiving an FDA-approved filler. And never get injectable fillers from unlicensed providers or in non-medical settings like hotels or private homes.
2. **ALWAYS** request and read the patient labeling information on FDA-approved injectable wrinkle fillers (/dermal-fillers-approved-center-devices-and-radiological-health) from your licensed health care provider.
3. **ALWAYS** know the type of product to be injected and all of its possible side effects. Know where each product used is to be injected. Talk to your licensed health care provider if you have any questions.
4. **NEVER** buy dermal fillers on the Internet. They may be fake, contaminated, and/or harmful.
5. **NEVER** get any type of filler or liquid silicone injected for body contouring. This means you should never get breast fillers, “butt” fillers, or fillers for spaces between your muscles. These products, which include certain types of injectable silicone, can be dangerous and can cause serious injury and even death.

Also know that the safety of these products is unknown for use in pregnant or breastfeeding women or in patients under 18 years of age. The safety also is unknown if used with Botox or other wrinkle therapies. (The FDA regulates Botox Cosmetic as a drug. See the section below for more information.)

ATTACHMENT D

You should discuss the different types of FDA-approved dermal fillers and the results you want to achieve with your licensed health care provider, who can refer you to a licensed dermatologist or plastic surgeon. (You may want to contact the American Academy of Dermatology (http://www.aad.org/) (http://www.fda.gov/about-fda/website-policies/website-disclaimer), the American Society of Plastic Surgeons (https://www.plasticsurgery.org/) (http://www.fda.gov/about-fda/website-policies/website-disclaimer), or the American Society for Aesthetic Plastic Surgery (https://www.surgery.org/) (http://www.fda.gov/about-fda/website-policies/website-disclaimer).)

Ask your licensed health care provider if you have specific questions.

More About Botox

Botox Cosmetic and other botulinum toxin type A products such as Dysport and Xeomin are indicated to treat wrinkles. Remember that they are injectable drugs but not dermal fillers. They work by keeping muscles from tightening so the wrinkles don't show as much. Adverse events reported in clinical trials include facial weakness, eyelid drooping, and brow drooping. Other adverse events included localized pain, swelling, reddening, and bruising at the injection site.

The FDA has approved these products only for the temporary improvement in the appearance of frown lines, forehead lines, and crow's feet. If you have questions about these products, talk to your licensed health care provider.

If you'd like to report suspected criminal activity related to FDA-regulated products, you can make a report on the FDA's website (https://www.accessdata.fda.gov/scripts/email/oc/oci/contact.cfm).

And if you ever have a problem with an FDA-regulated product—such as an injury or an issue with the way the product works—please report the problem to the FDA. The agency continues to track approved products for safety even after they've been sold. You can file a voluntary report by phone at 1-800-FDA-1088 or online at MedWatch, the FDA Safety Information and Adverse Event Reporting program (https://www.fda.gov/safety/medwatch/).

back to top

ATTACHMENT D

Original Investigation

Increased Risk of Litigation Associated With Laser Surgery by Nonphysician Operators

H. Ray Jalian, MD; Chris A. Jalian, JD; Mathew M. Avram, MD, JD

IMPORTANCE Controversy exists regarding the role of nonphysicians performing laser surgery and the increased risk of injury associated with this practice.

OBJECTIVE To identify the incidence of medical professional liability claims stemming from cutaneous laser surgery performed by nonphysician operators (NPOs).

DESIGN, SETTING, AND PARTICIPANTS Search of an online national database of public legal documents involving laser surgery by NPOs.

EXPOSURE Laser surgery by nonphysicians.

MAIN OUTCOMES AND MEASURES Frequency and nature of cases, including year of litigation, certification of provider and operator, type of procedure performed, clinical setting of injury, and cause of legal action.

RESULTS From January 1999, to December 2012, we identified 175 cases related to injury secondary to cutaneous laser surgery. Of these, 75 (42.9%) were cases involving an NPO. From 2008 to 2011, the percentage of cases with NPOs increased from 36.3% to 77.8%. Laser hair removal was the most commonly performed procedure. Despite the fact that approximately only one-third of laser hair removal procedures are performed by NPOs, 75.5% of hair removal lawsuits from 2004 to 2012 were performed by NPOs. From 2008 to 2012, this number increased to 85.7%. Most cases (64.0%) by NPOs were performed outside of a traditional medical setting.

CONCLUSIONS AND RELEVANCE Claims related to cutaneous laser surgery by NPOs, particularly outside of a traditional medical setting, are increasing. Physicians and other laser operators should be aware of their state laws, especially in regard to physician supervision of NPOs.

JAMA Dermatol. 2014;150(4):407-411. doi:10.1001/jamadermatol.2013.7117
Published online October 16, 2013.

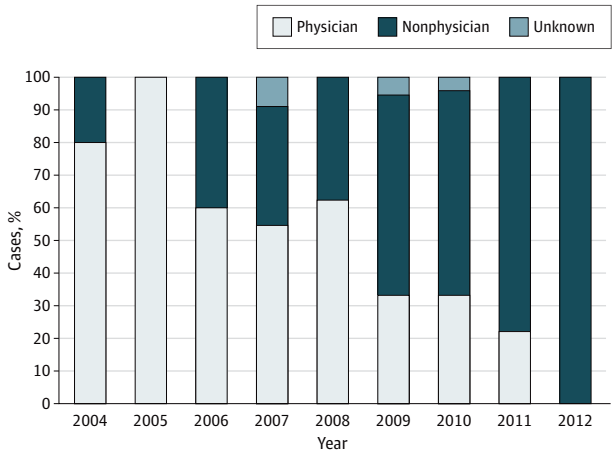
Author Affiliations: Division of Dermatology, University of California, Los Angeles (H.R. Jalian); Wellman Center for Photomedicine, Massachusetts General Hospital, Boston (H.R. Jalian, Avram); Paul Hastings, LLC, New York, New York (C.A. Jalian); Department of Dermatology, Harvard Medical School, Boston, Massachusetts (Avram).

Corresponding Author: H. Ray Jalian, MD, Division of Dermatology, University of California, Los Angeles, 2020 Santa Monica Blvd, Ste 570, Santa Monica, CA 90404 (hjalian@partners.org).

Cutaneous laser surgery remains one of the most popular elective procedures performed in the United States. Among dermatologic surgeons alone in 2011, more than 1.6 million laser treatments were performed.[1] Many more procedures were performed by physicians in other specialties and by nonphysician operators (NPOs). As the numbers of these procedures increase, a concomitant growth has occurred in laser injury-related litigation.[2] The practice of delegation to NPOs has accompanied the burgeoning trend toward greater availability of laser surgery and is hypothesized to be in part responsible for the increase in injury and litigation.[3] Moreover, the past decade saw the massive expansion of the so-called medical spas, nonmedical facilities offering aesthetic and cosmetic procedures.[4] Many of these facilities are owned by or retained by physicians; however, most of the procedures are performed by NPOs of varying certifications as permitted by state regulation. The degree of supervision varies among states, and often the physician supervisor is not required to be on the premises at the time of rendering of services.[5]

Many physicians are increasingly using physician extenders (PEs) within their practice to meet rising demand and falling reimbursements. Among dermatologists, almost 30% reported using a PE within their practice, a 40% increase over the preceding 5 years.[6] Although no data have emerged regarding increased litigation associated with this practice, legal precedence and numerous investigations are clear on liability.[7] When a physician delegates duties to a PE, responsibility and liability remain squarely on the supervising physician provided that the services rendered fall within the scope

Figure. Procedures Performed by Nonphysician Operators Increasingly Represent Most Lawsuits



The percentage of cases involving a nonphysician operator is expressed as a percentage of total operators per calendar year. Note the increasing trend toward a larger proportion of nonphysician operators starting in 2008.

of duty of the PE. This holds true for physician supervision of NPOs in the setting of cutaneous laser surgery.[2]

Despite these trends and clear inconsistencies in state regulations, no study to date has quantified the effect of these practices on medical professional liability claims with regard to cutaneous laser surgery. The objective of this study was to expand on previously published findings in an effort to identify high-risk practices that result in litigation. In addition, the study examines the incidence of litigation related to the performance of laser surgery by NPOs.

Methods

We searched the legal research resource WestlawNext (http://westlaw.com) using various keywords as previously reported.[2] This database is a primary source used by attorneys to gather legal information and is available by subscription to the public. Documents within this database are in the public record. The study was exempt from review, as determined by the institutional review board at Massachusetts General Hospital. An updated search yielded one additional case, bringing the total number of claims concerning injury resulting from cutaneous laser surgery to 175. Of these 175 cases, 75 of the procedures were performed by NPOs. For this study, an *NPO* is defined as a non-MD, non-DO provider. Because of the nature of the documents within the database, it is difficult to ascertain the exact certification of the NPOs. In an effort to be accurate, various allied health professionals comprised the NPO category. This included operators described as a *registered nurse* or a *nurse practitioner*, as well as terms such as *technician*, *aesthetician*, *assistant*, and *intern*. In addition to previously acquired data, the setting where services were rendered was recorded.

Results

NPO as a Function of Year of Litigation

Of 175 cases identified, the first occurrence of an NPO was in 1999. From January 1999, to December 2012, a total of 75 cases with NPOs were identified. This represents 42.9% of the total cases during the same time frame. Stratification of laser operator by year of litigation revealed a striking trend. From 2004 to 2012, a trend was observed toward an increased proportion of lawsuits stemming from cutaneous laser surgery performed by NPOs. This trend is most notable from 2008 to 2011, our most recent data, during which time the percentage of cases involving an NPO increased from 36.3% to 77.8%. Of the 2 cases in 2012, both were performed by an NPO. These results are summarized in the **Figure**.

Procedures

In line with our previously published data,[2] the most commonly performed procedure (n = 40) from 2004 to 2012 that resulted in injury and litigation by an NPO involved laser hair removal. Rejuvenation, composed mainly of intense pulsed light treatments, was the second most commonly litigated procedure (n = 7). Among the NPO cases, a notable trend is evident: when expressing the number of NPO cases as a percentage of the total number of cases for the same procedure, 75.5% of laser hair removal lawsuits from 2004 to 2012 were performed by an NPO. This number is even more dramatic in the years 2008 to 2012, when 85.7% of all laser hair removal lawsuits were performed by an NPO. From 2010 to 2012, a total of 90.0% (18 of 20) of laser hair removal cases were performed by an NPO. The remainder of the litigated procedures by NPOs and the proportion of total cases are given in **Table 1**.

Location of Services

From 1999 to 2012, a total of 64.0% (n = 48) of the NPO cases arose in a nonmedical practice setting. These include medical spas and other nonmedical facilities offering cosmetic services (eg, salons, spas, etc). In 2008 to 2011, NPO procedures performed in medical spas represented almost 80% of lawsuits. Of the 2 cases in 2012, one was performed in a medical spa setting and the other in a physician office. When looking at the type of procedure performed in this setting, most of these cases were laser hair removal procedures. From 2008 to 2012, a total of 68.6% (n = 24) of laser hair removal litigation cases involved an NPO in a medical spa setting. These results are summarized in **Table 2**.

Specific Allegations

Not surprisingly, the injuries sustained following laser surgery by NPOs and the causes of action in these cases mirror those previously reported by our group.[2] However, the specific allegations in these cases offer insight into various liabilities imposed on physician supervisors.

It is necessary to first examine the 2 different forms of liability (direct and vicarious) that a physician could face arising from allegedly improper laser treatment. A physician is directly liable for any negligence that can be attributed to an

ATTACHMENT D

Table 1. Cases Involving Laser Procedures Performed by Nonphysician Operators

Procedure	No./Total No. (%) All Cases[a] (n = 106)	All Cases by Nonphysician Operators 2004-2012[b]	All Cases by Nonphysician Operators 2008-2012[b]
Hair removal	40 (37.7)	40/53 (75.5)	30/35 (85.7)
Rejuvenation[c]	7 (6.6)	7/22 (31.8)	7/22 (31.8)
Leg veins	3 (2.8)	3/7 (42.9)	3/7 (42.9)
Vascular[d]	1 (0.9)	1/4 (25.0)	1/4 (25.0)
Tattoo	1 (0.9)	1/4 (25.0)	1/4 (25.0)
Scar	2 (1.9)	2/2 (100.0)	2/2 (100.0)
Pigmented lesion	1 (0.9)	1/1 (100.0)	1/1 (100.0)
Other[e]	2 (1.9)	2/3 (66.7)	2/3 (66.7)

[a] All cases from 2004 to 2012, including physician, nonphysician, and unknown operators.

[b] All nonphysician operator cases expressed as a percentage relative to the total specific procedure cases with all operators.

[c] Most with an intense pulsed light device.

[d] Includes treatment of vascular lesions and telangiectasia.

[e] Includes one case related to fat removal and one case of skin tightening.

Table 2. Setting of Cases Involving Laser Procedures Performed by Nonphysician Operators

Year	No./Total No. (%) Medical Spa	Physician Office	Unknown Setting	Laser Hair Removal[a]
1999-2012	48 (64.0)	25 (33.3)	2 (2.7)	33/48 (68.8)
2004-2012	41 (70.7)	16 (27.6)	1 (1.7)	29/40 (72.5)
2008-2012	36 (76.6)	11 (23.4)	0	24/35 (68.6)

[a] Number of cases performed by nonphysician operators in a medical spa setting relative to the total procedures performed by nonphysician operators in all settings.

individual capacity (ie, the personal failure to perform his or her duties at the requisite standard of care). A physician's duties often extend beyond the laser procedure; for instance, a physician may be directly liable for any negligent hiring, supervision, or training and so forth.

Conversely, a physician is vicariously liable for the negligence of his or her employees. A physician's vicarious liability is rooted in the doctrine of *respondeat superior* (Latin for "let the master answer"). This common law doctrine is often used to hold the employer responsible for the actions of his or her employees if and when the employee is acting within the scope of his or her employment. The rationale underpinning the application of vicarious liability to an employer is 2-fold. First, an employer has the ability and duty to control his or her employees. Second, presumably an employee is performing duties that will result in a benefit to the employer and in so doing is acting under the direction or authority of the employer. Therefore, in a medical malpractice context, a physician can be vicariously liable for the negligence of his or her subordinates, including nurses, NPOs, and other staff.

Almost all of the malpractice cases arising from the negligence of NPOs are coupled with vicarious liability claims against the employer, often a medical spa but at times a physician owner. Notably, 25 of 58 cases (43.1%) with NPOs from 2004 to 2012 represented instances in which no direct physician supervisor was identified. In these cases, the facility was often named as the defendant. As for a physician's direct liability in NPO cases, by far the most common specific allegation (n = 27) was failure to supervise the delegate. Failure to supervise represents the physician's failure to properly oversee the procedure. Failure to train and hire appropriate staff was the second most common specific allegation (n = 23). In addition to these allegations, negligent entrustment (n = 2) was alleged against the physician employers in their individual capacity. Negligent entrustment arises when one party (the entrustor) is held liable for providing another individual (the entrustee) with a potentially dangerous instrument. In this context, a physician can be held liable for providing an NPO with a laser if this instrument is used for a procedure that results in injury to a patient. The physician liability is predicated on the fact that a reasonable person in like circumstances would not have entrusted the NPO with the equipment. A summary of specific allegations (where available) relating to injury sustained as a result of laser surgery by NPOs from 1999 to 2012 includes the following: failure to properly hire, train, or supervise staff (n = 27); failure to properly perform treatment or operate a laser (n = 23); failure to conduct a test spot (n = 10); lack of a license to perform a procedure (n = 6); failure to recognize or treat an injury (n = 5); and negligent entrustment (n = 2). As can be seen from the foregoing definitions, a physician's direct liability is predicated on his or her negligence, not the negligence of his or her employee or agent.

Discussion

Physician delegation of laser surgery has grown significantly during the past decade. In addition, nonphysician-supervised NPO laser surgery is being performed legally in many states at nonmedical facilities. Data on the safety of NPO performance of cutaneous laser surgery are lacking in the medical literature. Most important, a clear trend demonstrates a dramatic increase in the number of lawsuits associated with NPO performance of laser surgery. The NPOs comprise a vast diversity of operators, including nurse practitioners, registered nurses, medical assistants, electrologists, and aestheticians, among others. In 2011, the latest year with a presumed complete data set, 77.8% of the cases involved an NPO. In addition, of the cases with NPOs, almost two-thirds occurred outside of a traditional medical practice. From an examination of

ATTACHMENT D

the specific allegations available in this study, the following 2 themes emerged: (1) both vicarious and direct liability of the supervising physician and (2) the prevalence of nonmedical personnel failing to perform procedures commensurate with the standard of care, including recognizing and treating complications.

We propose that the overall trend in increased litigation for laser surgery is in part explained by greater numbers of NPOs performing these procedures, in particular those practicing without direct supervision in the medical spas. This is the first study to date to offer such quantitative evidence. Of the procedures performed, laser hair removal accounted for most of these cases. Indeed, laser hair removal is the most frequently performed laser procedure in the United States.[8] However, if one takes into account the number of procedures performed by operators (physician vs NPO), the data become even more compelling. Only one-third of laser hair removal procedures in 2012 were performed by an NPO; the remaining two-thirds were performed by physicians.[8] Despite the fact that physicians perform most laser hair removal, 85.7% of laser hair removal lawsuits in our study from 2008 to 2012 are cases involving an NPO. In 2011, a remarkable 90.9%% (10 of 11) of laser hair removal litigation was against NPOs. One way to interpret these data is that some increased inherent risk of injury exists with an NPO.

The inconsistency and ambiguity of the state laws exemplify the lack of uniformity of the practice of delegation. For example, in Maine only a physician may operate a laser for hair removal. At the other end of the spectrum, Nevada as of June 2011 had no regulations regarding the use of a laser. In addition to the ability to delegate these procedures is the degree of supervision required. Some state statutes are explicit in stating the need for a written protocol, the requirement to appropriately train and document the training of personnel, and the necessity for adequate supervision. Many physicians "lend" their medical license to these facilities without meeting the legal requirements for supervision. In line with this, California recently passed a bill (California Assembly Bill 1548, Chapter 140) that increases penalties for illegally owning and operating a medical spa, with fines up to $50 000 and a maximum of 2 to 5 years in state prison. The lack of overarching federal law makes it difficult to uniformly require qualifications of personnel allowed to render laser treatments. Despite appropriate certification, regulations regarding appropriate training are ambiguous and are subject to interpretation. Because laws and regulations are constantly evolving, it is imperative for physicians who use PEs to be up to date. Current guidelines can be found at state medical board and state legislature websites.

In the correct setting, with close on-site supervision and appropriate training, the use of NPOs can prove to be a fruitful, productive, and safe environment for patients. Perhaps a larger issue is the role of NPOs, as well as physicians without adequate training, in the operation of a laser. Technology related to laser surgery has evolved rapidly since the description of selective photothermolysis by Anderson and Parrish[9] in 1983. Despite the propagation of nonmedical facilities performing these procedures, the tremendous amount of physics and medicine related to cutaneous surgery should not be overlooked. The American Society for Dermatologic Surgery Association position promulgates the use of energy devices capable of altering or damaging living tissue to physicians who are "trained appropriately in the physics, safety, and surgical techniques involved in the use of energy devices capable of damaging living tissue prior to performing procedures using such devices."[10] Moreover, in the setting of delegation, a physician "should be fully qualified by residency training and preceptorship or appropriate course work prior to delegating procedures to licensed allied health professionals and should directly supervise the procedures. The supervising physician shall be physically present on-site, immediately available, and able to respond promptly to any question or problem that may occur while the procedure is being performed."[10] Finally, the position statement underscores the need for "appropriate documented training in the physics, safety, and surgical techniques of each system. The licensed allied health professional should also be appropriately trained by the delegating physician in cutaneous medicine, the indications for such surgical procedures, and the pre- and post-operative care involved in treatment."[10]

Several limitations are inherent in conducting research using a legal database. First, although it is a massive data bank, only one legal database was searched. Cases within the database are those in which some form of legal action was taken and exclude complaints handled outside of the judicial system (ie, third-party arbitration through a malpractice carrier). This is likely to have excluded many frivolous claims with little merit. Second, the query was a retrospective review and was limited by the search terms selected; it is likely that some decisions exist that did not contain the searched terms. Third, these legal pleadings are layman documents (ie, not medical records), and the veracity of the facts was assumed to be true. Furthermore, layman terms may have eluded a database search for the purposes of this study. Fourth, because of the limited number of cases with NPOs for certain procedures, it is difficult to interpret the trends for less commonly performed surgery. Nonetheless, the actual data likely understate the true incidence of NPO laser complications. Generally, plaintiffs' attorneys do not pursue litigation against uninsured operators. Unlike physicians, NPOs (especially in a nonmedical office setting) are less likely to possess liability insurance that can satisfy a potential malpractice or other legal judgment.

A dramatic increase in litigation has been filed against NPOs performing cutaneous laser procedures in medical and nonmedical office settings. This has important implications for the safety of patients undergoing these procedures. When a physician delegates duties to a PE, responsibility and liability remain squarely on the supervising physician provided that the services rendered fall within the scope of duty of the PE. This holds true for physicians supervising NPOs in the setting of cutaneous laser surgery. Given the increase in NPO laser surgery procedures and a parallel trend in greater frequency of lawsuits, further studies are needed to examine this troubling trend in laser safety.

ARTICLE INFORMATION

Accepted for Publication: July 21, 2013.

Published Online: October 16, 2013. doi:10.1001/jamadermatol.2013.7117.

Author Contributions: Dr H. R. Jalian had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: H. R. Jalian, Avram.
Acquisition of data: H. R. Jalian, C. A. Jalian.
Analysis and interpretation of data: All authors.
Drafting of the manuscript: All authors.

Conflict of Interest Disclosures: Dr Avram serves as a member of the medical advisory board for Zeltiq Aesthetics, Inc, and of the scientific advisory board for Cytrellis Biosystems, Inc. He has served as a consultant for Unilever, Zeltiq Aesthetics, Inc, and Allergan within the past 12 months. No other disclosures were reported.

REFERENCES

1. American Society for Dermatologic Surgery. ASDS survey results demonstrate broad scope of practice for dermatologic surgeons. http://asds.net/_Media.aspx?id=6966. Accessed September 7, 2013.

2. Jalian HR, Jalian CA, Avram MM. Common causes of injury and legal action in laser surgery. *JAMA Dermatol*. 2013;149(2):188-193.

3. Brody HJ, Geronemus RG, Farris PK. Beauty versus medicine: the nonphysician practice of dermatologic surgery. *Dermatol Surg*. 2003;29(4):319-324.

4. International Spa Association. The U.S. spa industry: fast facts. http://experienceispa.com/media/facts-stats/. Accessed March 16, 2013.

5. Choudhry S, Kim NA, Gillum J, et al. State medical board regulation of minimally invasive cosmetic procedures. *J Am Acad Dermatol*. 2012;66(1):86-91.

6. Resneck JS Jr, Kimball AB. Who else is providing care in dermatology practices? trends in the use of nonphysician clinicians. *J Am Acad Dermatol*. 2008;58(2):211-216.

7. Nestor MS. The use of mid-level providers in dermatology: a liability risk? *Semin Cutan Med Surg*. 2005;24(3):148-151.

8. Press Center. Statistics. http://surgery.org/media/statistics. Accessed May 21, 2012.

9. Anderson RR, Parrish JA. Selective photothermolysis: precise microsurgery by selective absorption of pulsed radiation. *Science*. 1983;220(4596):524-527.

10. American Society for Dermatologic Surgery Association. American Society for Dermatologic Surgery Association position on the use of energy devices capable of altering or damaging living tissue. http://asdsa.asds.net/m/position/Laser-Procedures/. Accessed September 4, 2013.

NOTABLE NOTES

The Men or Women Behind Nevi: Alfred Guido Miescher

Fabrizio Vaira, MD; Gianluca Nazzaro, MD; Carlo Crosti, MD; Stefano Veraldi, MD

The man behind Miescher nevus is Alfred Guido Miescher. He was born on November 4, 1887, in Naples, Italy. His mother was Marietta Berner, and his father, Max Eduard Miescher, was a businessman. He was the nephew of Johannes Friedrich Miescher (1844-1895), professor of pathophysiology at the University of Basel, Switzerland, and discoverer of nucleic acids. After the father's death, he followed his mother to Basel, her hometown, where Guido completed his school.

He started his studies in engineering at the *Eidgenössische Technische Hochschule* in Zurich, Switzerland, and then switched to medicine, studying in Basel, Zurich, and Munich, Germany.[1] Working as an assistant of the dermatologist Bruno Bloch, he wrote his thesis on a case of mycetoma. In 1933, after the death of his mentor, Miescher become professor and director of the University Dermatology Clinic in Zurich. Miescher was an excellent clinician, and he was passionate about clinical dermatology and Dermatopathology. Indeed, he said that "Dermatology is more than morphology."[1]

In his original landmark work, *Histologie de 100 cas de naevi pigmentaires d'après les methods de Masson*, published in 1935, Miescher studied 100 hemispherical naevi found mostly on women's' faces. They are dome-shaped papules in which melanocytes are distributed mostly endophytically, often in a wedge, and they reach the deep reticular dermis.[2,3] Miescher was a pioneer in the treatment of skin diseases with phototherapy and of cutaneous tumors with ionizing radiation. Indeed, he helped to improve dermatological radiotherapy, through determining the safest doses and innovative fractionation schemes to reduce the toxic effects. Miescher was skilled in identifying new aspects of already known diseases. He reclassified granulomatosis disciformis chronica et progressiva, and, in 1945, he was the first to describe the cheilitis granulomatosa, subsequently also called Miescher cheilitis.

His students said that he cared about only 3 things: dermatology, music, and mountains. Miescher was a gifted cellist and a lover of mountaineering, as well as an illustrious dermatologist. He bravely climbed numerous Swiss peaks. But his most important venture was an expedition to the Caucasus Mountains. Miescher was the first person to climb Mount Elbrus (5629 m) and ski down. After a life full of medical and sporting achievements, he fought against the cancer and died in 1961.

Author Affiliations: Università degli Studi di Milano, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano, Italy.

Corresponding Author: Gianluca Nazzaro, MD, Dipartimento di Fisiopatologia Medico-Chirurgica e dei Trapianti, Università degli Studi di Milano–Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico–Milano, Italy, Via Pace, 9 Milano, Italy (gianluca.nazzaro@gmail.com).

1. Löser C, Plewig G, Burgdorf WHC, eds. *Pantheon of Dermatology: Outstanding Historical Figures*. Berlin, Germany: Springer; 2013.

2. Ackerman AB, Magana-Garcia M. Naming acquired melanocytic nevi: Unna's, Miescher's, Spitz's, Clark's. *Am J Dermatopathol*. 1990;12(2):193-209.

3. Fernandez-Flores A, Sanchez-Velicia L, Manjon JA, Alija A, Soto F. A hypothesis on the morphologic differences between Unna and Miescher nevi on the head and neck, based on embryologic bases. *Am J Dermatopathol*. 2012;34(6):602-606.

ATTACHMENT D

December 2, 2024

William M. Perkins
Executive Director
Alabama Board of Medical Examiners
848 Washington Avenue
Montgomery, AL 36104

RE: Oppose Botulinum Toxin A and Dermal Fillers for Cosmetic Purposes Scope of Practice Expansion

Dear Mr. Perkins:

On behalf of the American Academy of Dermatology Association and the American Society for Dermatologic Surgery Association representing more than 17,000 dermatologists nationwide, we are writing to share our concerns with proposals that request the Alabama Board of Medical Examiners to authorize certified registered nurse practitioners (CRNP), physician assistants (PA) and registered nurses (RN) to administer botulinum toxin A and dermal fillers for cosmetic purposes.

Procedures by any means, methods, devices or instruments that can alter or cause biologic change or damage the skin and subcutaneous tissue constitute the practice of medicine and surgery. This includes the use of foreign or natural substances by injection or insertion. [i,ii] Our organizations believe that medical procedures using a Food and Drug Administration (FDA)-regulated device, such as those that can alter or cause biologic change or damage, should only be performed by a physician or appropriately trained non-physician personnel under the direct, onsite supervision of an appropriately trained physician.[iii] These proposals jeopardize patient safety and disregard what is considered adequate and appropriate medical education and training. Quality patient care includes evaluating a patient's needs and condition(s), selecting an appropriate course of treatment and providing adequate follow-up care.

With the growing public demand for facial fillers and neuromodulators, providing patients with properly trained, educated, and supervised medical personnel is a safeguard Alabama should have for its citizenry. Fillers and neuromodulators can also be used to treat scars from injury and surgery, as well as from medical conditions; other applications include correcting facial asymmetries resulting from congenital, accidental, or medical conditions. Our utmost concern is to ensure that these products are safely administered by licensed and qualified physicians or under the direct, on-site supervision of a licensed and qualified physician. "As with other cutaneous procedures, it is necessary to receive adequate training before using soft-tissue augmentation agents. Physician injectors should first be made to demonstrate a detailed knowledge of anatomy and possible adverse events (such as sensitivity, infection, and necrosis) through passing an American Board of Medical Specialties (or an ABMS-equivalent Board) examination in one of the CORE aesthetic specialties after residency training in one of these disciplines." [iv]

There are substantial differences in the education of non-physicians and physicians, both in depth of knowledge and length of training. Board certified dermatologists diagnose and treat over 3,000 different diseases and conditions. Dermatologists see patients of all ages – from newborns to the elderly. A board certified

dermatologist undertakes a minimum of 8 years of exhaustive medical education and training (4 years of medical school, 1 year of internship, 3 years (minimum) of dermatology residency), during which they complete 12,000 to 16,000 hours of direct patient care, before they can practice independently. Dermatologists must pass 3 standardized USMLE training exams to become licensed physicians and then pass a comprehensive examination at the conclusion of their residency training to become board certified in dermatology. Dermatologists have focused training in using fillers and neuromodulators involving the skin and adjacent structures, which prepares them to perform medical procedures using fillers and neuromodulators safely and effectively. Included in this training is proper technique, and the management of any adverse events.

In contrast, non-physicians have less clinical experience than a physician obtains in just the first year of a three-year medical residency. CRNPs obtain 500 to 720 hours of direct patient care, and PAs obtain 2,000 hours of clinical rotations after completing a 26-month program. These rotations emphasize primary care in ambulatory clinics, physician offices and acute or long-term care facilities.[v] Unlike physicians, non-physicians are not required to complete a residency program or demonstrate competency in procedures involving skin and soft tissue augmentation with products that can alter or damage living tissue. It is of upmost importance that the physician or non-physician performing procedures with neurotoxins (such as botulinum toxin) or dermal fillers have specific, long-term training (such as a medical residency in dermatology or plastic surgery). The education for non-physicians does not include this type of intense training; additionally, any short-term training program offered by manufacturers of these products does not adequately protect patient safety.

During a 2021 meeting of the FDA's General and Plastic Surgery Committee on Soft-Tissue Fillers, the American Society for Dermatologic Surgery's Task Force on Soft-Tissue Fillers found that knowledge of vascular anatomy is *crucial* for all filler injections. **Intravascular injection is possible at any location on the face, but certain locations carry a higher risk, such as filler embolization; necrosis; visual abnormalities; blindness; and stroke.**[vi] Thus, we are in firm agreement with the FDA's further updated consumer guidance in 2023 that anyone considering a neurotoxin or dermal filler consult with a licensed provider who is experienced in injecting dermal fillers, knowledgeable about fillers, anatomy, managing complications and knows the risks and benefits of treatment.[vii] Furthermore, the American Medical Association (AMA) states that, "Cosmetic medical procedures, such as botulinum toxin injections, dermal filler injections, and laser and intense pulsed light procedures, be considered the practice of medicine."[viii]

To best protect the citizens of Alabama from adverse events and ensure quality patient care, **we respectfully ask that the Alabama Board of Medical Examiners oppose the request to expand the scope of practice of CRNPs, PAs and RNs to include the administration of botulinum toxin A and dermal fillers for cosmetic purposes.** Thank you for your strong consideration on this matter. Should you have any questions regarding this critical patient safety issue, please do not hesitate to contact Kristin Hellquist, Chief Advocacy Officer at the American Society for Dermatologic Surgery Association, at khellquist@asds.net.

Sincerely,

American Academy of Dermatology Association
American Society for Dermatologic Surgery Association

---

[i] ASDSA *Position Statement on the Practice of Medicine*. https://www.asds.net/Portals/0/PDF/asdsa/asdsa-position-statement-definition-of-the-practice-of-medicine.pdf

[ii] AADA *Position Statement on Medical Spa Standards of Practice*. https://www.aad.org/Forms/Policies/Uploads/PS/PS-Medical%20Spa%20Standards%20of%20Practice.pdf

[iii] ASDSA *Position Statement on Delegation*. https://www.asds.net/Portals/0/PDF/asdsa/asdsa-position-statement-delegation.pdf

[iv] Gladstone H, Cohen J. Adverse Effects When Injecting Facial Fillers. Semin Cutan Med Surg. 2007 Mar;26(1):34-9.

[v] How are PAs Educated and Trained? https://www.aapa.org/what-is-a-pa/#tabs-2-how-are-pas-educated-and-trained

ATTACHMENT D

[vi] Jones D, Fitzgerald R, Cox S, Butterwick K, et al. Preventing and Treating Adverse Events of Injectable Fillers: Evidence-Based Recommendations From the American Society for Dermatologic Surgery Multidisciplinary Task Force. Dermatol Surg 2021;47:214-26.
[vii] Filling in Wrinkles Safely. Accessed Aug. 6, 2024. Retrieved from https://www.fda.gov/ForConsumers/ConsumerUpdates/ucm049349.htm
[viii] Addressing Safety and Regulation in Medical Spas. Retrieved Aug. 6, 2024. https://policysearch.ama-assn.org/policyfinder/detail/dermal%20fillers?uri=%2FAMADoc%2Fdirectives.xml-0-1174.xml

Review Article

Litigation Arising From Minimally Invasive Cosmetic Procedures: A Review of the Literature

Brian P. Hibler, MD,*† Philip J. Eliades, MD,‡ Karen C. Kagha, MD,*† and Mathew M. Avram, MD, JD*

BACKGROUND Minimally invasive cosmetic procedures are on the rise. To meet this rising demand, increasing numbers of physicians and nonphysicians are performing these procedures. Understanding malpractice trends and reasons for litigation in cosmetic medicine is important to establish safeguards for patient care and minimize liability.

OBJECTIVE Perform a comprehensive review of the literature on litigation associated with minimally invasive cosmetic procedures and discuss strategies to avoid facing a lawsuit.

MATERIALS AND METHODS The authors searched PubMed databases using a variety of keywords to identify studies of lawsuits arising from minimally invasive cosmetic procedures through December 2020.

RESULTS A total of 12 studies of litigation meeting inclusion criteria were identified: botulinum toxin (1), soft tissue fillers (3), lasers (5), body contouring/liposuction (1), chemical peels/dermabrasion (1), and sclerotherapy (1). Principle factors associated with litigation included negligence, lack of informed consent, vicarious liability for action of delegates, lack of communication, poor cosmetic result, failure to inform of risks, inappropriate treatment or dose, and failure to recognize or treat injury.

CONCLUSION Understanding malpractice trends and reasons for litigation in minimally invasive cosmetic procedures can strengthen the patient–provider relationship, establish safeguards for patient care, and may minimize future risk of a lawsuit.

Minimally invasive cosmetic procedures (MICPs) are on the rise. An American Society for Dermatologic Surgery (ASDS) member survey in 2018 revealed that dermatologists performed 3.7 million minimally invasive injectable cosmetic procedures, 3.49 million laser-based and light-based treatments, and over 600,000 body contouring procedures.[1] Dermatologists have pioneered the innovation and development of most noninvasive procedure or MICP[2]; however, to address this surging demand, increasing numbers of physicians and nonphysicians without accredited training in cosmetics are performing these procedures.[3]

With increasing numbers of nonsurgical and surgical cosmetic treatments being performed, a concomitant rise in complications and lawsuits has been observed for various procedures.[4–6] Approximately, half of all medical malpractice claims result in litigation, which can be expensive, time-consuming, emotionally stressful, and harmful to professional reputation.[7] Understanding malpractice trends and reasons for litigation in aesthetic medicine is important to establish safeguards for patient care and minimize liability.[8] Herein, the authors review the literature on litigation associated with MICP, highlight cases ruled in favor of the plaintiff, and provide strategies to avoid facing a lawsuit.

Methods

The authors searched PubMed for studies of lawsuits stemming from MICP through December 2020 published in English. Search terms included: "litigation" OR "malpractice" AND each of the following "cosmetic," "botulinum toxin," "neurotoxin," "filler," "laser," "liposuction," "body contouring," "dermabrasion," "chemical peel," "sclerotherapy," "cryolipolysis," "radiofrequency," "ultrasound," "hair transplant." Articles were reviewed for content and discussion of litigation and MICP. Individual cases were cross-referenced using Westlaw and Google Case Law databases. Studies of lawsuits from cosmetic surgery without subgroup analysis of MICP (laser resurfacing, cosmetic injectables) are referenced but not discussed in detail as it is beyond the scope of this article.

Results

Seventeen studies of litigation were identified: botulinum toxin (1), soft tissue fillers (3), lasers (5), body contouring/liposuction (6), chemical peels/dermabrasion (1), and sclerotherapy (1). Five body contouring studies included chiefly cosmetic plastic surgery (e.g., breast augmentation, abdominoplasty, rhinoplasty, and more invasive cosmetic procedures) and were omitted from detailed analysis. The remaining 12 studies met inclusion criteria.

*From the *Department of Dermatology, Dermatology Laser and Cosmetic Center, Massachusetts General Hospital, Boston, Massachusetts; †Wellman Center for Photomedicine, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts; ‡Schweiger Dermatology Group, New York City, New York*

The authors have indicated no significant interest with commercial supporters.

Address correspondence and reprint requests to: Brian P. Hibler, MD, Dermatology Laser and Cosmetic Center, Massachusetts General Hospital, 50 Staniford Street, Suite 250, Boston, MA 02114, or e-mail: BrianHibler@gmail.com

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.dermatologicsurgery.org).

http://dx.doi.org/10.1097/DSS.0000000000003202

Major allegations and their definitions are summarized (See **Supplemental Digital Content 1**, Table S1, http://links.lww.com/DSS/A890) to serve as a reference throughout the Results section.

Botulinum Neurotoxin

Litigation

In 2018, ASDS members performed over 2 million neuromodulator procedures, a 42% increase since 2012.[1] Although botulinum neurotoxin (BN) has an excellent safety profile, its widespread use and ever-expanding indications have raised some concerns about patient safety.

Korman and colleagues[9] reviewed litigation between 1985 and 2012 involving alleged adverse events (AEs) arising from cosmetic or therapeutic uses of BN. They identified 24 cases, with the majority occurring at the state level; of note, 17 cases were part of a mass tort in California. Allergan, the producer of Botox, was a defendant in all cases. Physicians were codefendants in 3 cases; 1 was a dermatologist. There were 5 times as many lawsuits involving therapeutic use compared to cosmetic application. Overall, 10 claims were dismissed and settlement was reached in 6. Of 5 cases tried before a jury, only 2 were decided in favor of the plaintiff (Table 1).

Protecting Yourself

The small number of cases identified probably underestimates the actual total (see Limitations), but is still notable given that millions of procedures are performed annually. Nevertheless, the scarcity of lawsuits may be due in part to an overall low rate of serious AE,[9,10] and the transient nature of toxin effect typically resulting in self-resolving AE.

More lawsuits seen with therapeutic BN are likely due to greater average dosages administered and underlying patient comorbidities.

Reviewing potential risks of BN (including risk of systemic involvement from distant spread), withholding treatment in setting of known contraindications, and ensuring not to exceed maximum safe dosages (including asking about recent treatment and if they are getting BN for other indications, e.g., migraines) may reduce risk of future legal action.[11]

Soft Tissue Fillers

Litigation

Soft tissue fillers are increasingly popular to address volume loss and facial rejuvenation, and are the second most common injectable cosmetic procedure performed by dermatologic surgeons.[1] While the safety profile is generally favorable, complications and resultant litigation may occur.[12,13]

Three studies evaluated litigation with injectable fillers. Ezra and colleagues[12] reviewed the Westlaw database through 2013 and identified 19 cases. Physicians were defendants in 13 cases (68%), manufacturers in 11 (58%), and clinics and nonphysicians in 7 each (37%); many lawsuits named multiple defendants. Overall, 50% of legal actions from fillers were related to nonphysician injectors. Often, disciplinary action was taken for physicians not being present while nonphysicians injected patients, frequently in the medical spa setting.

In a second study, Rayess and colleagues[14] reviewed the Westlaw database for medical malpractice related to facial soft tissue fillers. They identified 9 cases; 4 resulted in payment, with 2 decided in favor of the plaintiff (Table 1) and 2 settled. Six cases (67%) alleged inadequate informed consent, with half resulting in payment to the plaintiff. Five cases (56%) alleged permanent injury, 2 from intra-arterial injection and one of which caused blindness. In 5 cases (56%), plaintiffs alleged the filler choice or procedure was inappropriate/contraindicated.

Most recently, Beauvais and Ferneini[15] reviewed litigation for facial injectable filler cases from 2008 to 2017 using Westlaw. Eleven cases containing verdicts were included. Five cases (45%) resulted in payment to the plaintiff (range 349 k–1060 k); 4 cases were decided in the plaintiff's favor (Table 1) and 1 case was settled. Overlap exists between the cases presented by Rayess and colleagues and Beauvais and Ferneini; 2 cases resulting in payment appear in each. Fillers included: Restylane (3), Radiesse (2), Sculptra (2), Juvederm (1), Evolence (1), hydroxyapatite (1), and unknown (1). Four of the 5 noting location of injection were periocular. All but one case (91%) alleged lack of informed consent. Alleged complications ranged from swelling/lumps to nerve damage to permanent blindness; 7 (64%) alleged permanent injury.

Protecting Yourself

The literature on soft tissue filler litigation, albeit limited and likely severely underestimated by not accounting for cases settled out of court, suggests that successful lawsuits are exceedingly uncommon. Lack of informed consent was alleged in most lawsuits, including 6 of the 7 cases decided in favor of the plaintiff. Several common, temporary complications can arise from soft tissue fillers (e.g., bruising, swelling, nodules, infection); however, the rare complications, such as vascular occlusion and resultant scarring, blindness, or nerve damage, are often raised in malpractice lawsuits.[14] These rare, but serious risks should be included in the consent process.

An understanding of anatomy, facial vasculature, and safe injection technique is critical to prevent intra-arterial complications.[16,17] Overseeing mid-level providers increases a physician's exposure to litigation[12] (see: Vicarious Liability, See **Supplemental Digital Content 1**, Table S1, http://links.lww.com/DSS/A890). Physicians can be held liable for failure to adequately supervise delegates, and the standard of care in nontraditional settings (e.g., medical spa, salon) is no different from medical offices.[18]

Lasers

Litigation

Advancements in laser surgery have allowed for treatment of numerous medical and cosmetic concerns.[19] However, with increasing use of laser technology has come a concomitant increase in lawsuits alleging malpractice.

TABLE 1. Cosmetic Injectable Litigation Cases Decided in Favor of Plaintiff (Adapted From Korman and Colleagues, Rayess and Colleagues, and Beauvais and Ferneini)[9–11]

	Age/ Sex	Defendant	Product	Location/ Procedure	Alleged Complication	Lack of Informed Consent	Award (Thousands, $)
Neurotoxin			Botox	Cosmetic	Systemic botulism (muscle weakness, paralysis, respiratory problems, pain)		15
			Botox	Therapeutic	Severe immune reaction and brain injury		212
Filler	60, F		Restylane	Periorbital	Pierced blood vessel, permanent facial disfiguration	Yes	750
	F	Aesthetician	Foreign product (not specified)	Eyebrows	Swelling, lumps	Yes	349
	F		Radiesse	Unspecified	Scarring	Yes	1,060
	F		Radiesse	Unspecified	Nerve damage, visual impairment, infection	Yes	600
	48, F	Plastics	Juvederm	Temple	Permanent blindness	No	425
	F	Physician & nurse	Collagen	Glabella	Supratrochlear injection resulting in pain and necrosis	Yes	175
	F	Otolaryngologist	Silicone	Periorbital	Postinjection swelling	Yes	21

F, female.

Jalian and colleagues[4] searched the Westlaw database for medical professional liability claims from cutaneous laser surgery. Between 1985 and 2012, there were 174 cases identified, with an overall trend of increasing cases. The most represented specialties were plastic surgery (25.9%) and dermatology (21.3%). A physician operated the laser in 100 cases but was named as defendant in 146 cases. Litigation most commonly resulted from laser procedures for hair removal (36.2%), rejuvenation (24.7%) (intense pulsed light [IPL], nonablative and ablative resurfacing), vascular lesions (8%), leg veins (7.5%), and tattoo removal (6.9%). Injuries included burns (47%), scars (38.8%), pigmentary alterations (23.5%), and disfigurement (15.8%). The most common accusation was lack of informed consent (30.5%). Allegations of psychological injuries were prevalent, including emotional distress (11.5%), diminished quality of life (3.8%), and embarrassment (2.7%). Of 120 cases with available disposition, 61 (50.8%) resulted in plaintiff recoveries (32 through motion, judgment, or jury verdict and 29 settled out of court).

In a follow-up study, Jalian and colleagues[20] investigated the increased risk of litigation associated with laser surgery by nonphysician operators (NPOs), including nurses, nurse practitioners, chiropractors, podiatrists, technicians, and aestheticians. They utilized the previously reported dataset[4] with one additional case identified. Nonphysician operators were defined as any non-MD/DO provider. Of the 175 cases, 75 (43%) were performed by NPOs. From 2008 to 2011, the percentage of cases with NPOs increased from 36.3% to 77.8%. Laser hair removal was by far the most common procedure, followed by rejuvenation (mainly IPL). Most cases (64%) were performed outside of a traditional medical setting (e.g., medical spa, salon). The most common allegations against physicians in cases of NPOs included failure to supervise, followed by failure to train and hire appropriate staff.

Pierce and Martell[21] reviewed the LexisNexis database from 1991 to 2015 for medical malpractice with ablative laser surgery. Forty-two cases were identified, but did not distinguish between fractionated/nonfractionated therapies. Five cases (12%) were settled and 8 cases (19%) rendered verdicts in favor of the plaintiff, citing: inadequate informed consent (55%), inappropriate treatment/dose (18%), and failure to warn (9%). Scarring (57%), discoloration (14%), and infection (9.5%) were the most common alleged injuries.

Svider and colleagues[22] evaluated litigation after head and neck laser procedures. They reviewed the Westlaw database and identified 34 cases between 1992 and 2013; dermatologists were most frequently named (32%)

followed by otolaryngologists (18%) and plastic surgeons (18%). There were several rhinologic and airway cases; however, cutaneous procedures, including antiaging, acne scarring, and hair removal, totaled 74% of cases. Overall, 56% rendered a defendant verdict. Of cases with a dermatologist defendant, 7 resulted in favor of the dermatologist, 2 were settled, and 2 were in favor of the plaintiff (Table 2). Frequent allegations included permanent injury, disfigurement/scarring, inadequate informed consent, and unnecessary/inappropriate procedures. Allegations of inadequate informed consent were raised in 50% of cases; 10 of these 17 cases resulted in a payment.

Halepas and colleagues[6] reviewed the Westlaw database for light-based skin resurfacing procedures between 1999 and 2019. Cases were excluded if dismissed or settled outside of court. Nine lawsuits were identified; common allegations included negligence (88.8%), cosmetic deformity (77.7%), and lack of informed consent (55.5%). Four cases (44.4%) were ruled in favor of the plaintiff, with an average award of $656,000. Two defendants were dermatologists, but only 1 successfully defended their lawsuit. The other 3 cases ruled in favor of the plaintiff involved an ophthalmologist, general surgeon, and internist.

Protecting Yourself

Multiple themes emerge when reviewing studies of litigation with laser surgery. Inadequate informed consent is among the leading causes of malpractice litigation in cosmetic laser treatments and may stem from patient's expectations not being met or insufficient pretreatment discussion of risks. Discussion of the potential need for additional treatments may decrease liability.

Other common allegations included failures to warn/inform of risk, select appropriate laser settings, and recognize and treat injury.[4] As with other MICPs, patient counseling should include both the most common and the severe AEs. Although often used to treat scarring, the risk of laser-induced scars should be addressed.[21] Burns and dyspigmentation were other frequent alleged injuries, often seen in litigation favoring the plaintiff (Table 2). There were 4 cases of ocular injury, reiterating the importance of proper eye protection and implementation of laser checklists.[4,23]

Various specialists were named in laser lawsuits, raising concern regarding appropriate training and scope of practice.[4,6] Physicians without specific training in medical laser devices are held to the same standard of care expected of well-trained physicians. As such, providers wishing to offer cosmetic laser treatments should obtain requisite training and/or licensing.[4]

Increasing laser litigation is at least partly attributable to untrained NPOs. Under the doctrine of *vicarious liability*, a physician may be directly liable if an NPO performs a delegated procedure resulting in injury.[20] Physicians should be aware of their state laws regarding NPO supervision.[24] Even if supervision is not required, physicians may still be liable for the misconduct of their delegates. The ASDS supports direct, on-site supervision of licensed and properly trained nonphysicians performing nonablative laser procedures, with clear and transparent communication with the patient about who will be providing care.[25] In contrast, however, the ASDS position is that only properly trained physicians should be injecting dermal fillers and neuromodulators.[26]

The most common delegated procedure leading to lawsuits was laser hair removal. Providers must evaluate skin type, select appropriate parameters, and consider using a test spot prior to treatment. Other studies have echoed these observations, with significant complications occurring from laser hair removal and IPL treatment by laypersons.[27]

TABLE 2. Laser Litigation Decided in Favor of Plaintiff (Compiled From Halepas and Colleagues and Svider and Colleagues)[6,22]

Case	Age/Sex	Defendant	Laser	Indication	Alleged Complication	Lack of Informed Consent	Award (Thousands, $)
1	52, F	Dermatologist	Carbon dioxide	Skin resurfacing	Perioral scarring, third-degree burn, dyspigmentation	Yes	977
2	F			Facial telangiectasias	Ulcers and scarring	Yes	80
3	F	Ophthalmology		Skin resurfacing	Skin necrosis	No	1,265
4	F	General surgeon		Skin resurfacing	Hypopigmentation	No	132
5	F	Internist		Skin resurfacing	Burns	No	250

F, female.

Body Contouring

Litigation

Body contouring procedures have dramatically increased in the past decade.[1] Among dermatologic surgeons, the most commonly performed include cryolipolysis, radiofrequency, and deoxycholic acid injections. Tumescent liposuction continues to be routinely performed, and newer technologies including laser lipolysis, microfocused ultrasound, and novel cellulite treatments are emerging to address tissue tightening and silhouette concerns in a minimally invasive fashion.

No studies to date have evaluated litigation with ultrasound or radiofrequency devices, deoxycholic acid injections, or laser lipolysis or cryolipolysis.

Coleman and colleagues[28] reviewed malpractice claims involving liposuction from the Physicians Insurance Association of America database from 1995 to 1997. Overall, 257 claims were identified, involving plastic surgeons in 226 claims (88%), general surgeons in 19 (7.4%), obstetrics/gynecology in 4 (1.6%), family practitioners in 2 (0.8%), and dermatologists in 2 (0.8%). Most procedures occurred in the hospital (71%) as compared with outpatient office (21%) or surgery centers (8%), despite most cosmetic surgery being performed in the office or ambulatory surgery centers. However, the authors note that larger, more risky liposuction cases are more likely to be performed in the hospital. This study did not examine final verdicts or settlements of the malpractice claims.

There are studies evaluating litigation related to cosmetic surgery[5,29,30]; however, a lack of detailed subgroup analysis of litigation pertaining solely to MICP limits their applicability. The major allegations are chiefly the same, including negligence, issues of consent, poor cosmetic result, scarring, and lack of supervision or appropriate training.[29,30] Claims of pain and emotional distress after facial plastic surgery correlate with a plaintiff verdict.[29]

Consistent with studies in the United States, litigation for plastic surgery in Australia and South Korea often stem from alleged lack of informed consent, failure to disclose particular risks, and potential lack of benefit not being explained.[31,32] These studies also included MICP but lacked explicit detail. Scarring, need for reoperation, pain, and nerve damage were the most common AE or causes of dissatisfaction.[31,32]

Protecting Yourself

Minimally invasive techniques to address body contouring concerns are expanding. However, studies of litigation are limited to liposuction and invasive surgical techniques. Tumescent liposuction, introduced by dermatologist Jeffrey Klein, is performed under local anesthesia, offering quick recovery and excellent outcomes.[33] This technique decreases bleeding and its safety has been well documented.[34–36] Performing small-volume liposuction under tumescent anesthesia has resulted in less injury and consequently fewer malpractice settlements.[28] Detailed record keeping, including digital photography and any postprocedural contact, is an important safeguard.[37] American Society for Dermatologic Surgery "Guidelines of Care for Tumescent Liposuction" offer education to safely perform the procedure along with postprocedural recommendations to optimize outcomes.[38]

Chemical Peels and Dermabrasion

Litigation

Chemical peels and dermabrasion are common procedures for facial skin resurfacing and rejuvenation. Complications can arise from deeper chemical peels and overly aggressive treatment.

Svider and colleagues[39] examined the Westlaw database between 1992 and 2012 for medical malpractice from chemical peels or dermabrasion (Table 3). Twenty-five cases were analyzed. Plastic surgeons were defendants in 12 cases and dermatologists in 6 cases, with various other specialties represented; 2 cases named aestheticians as codefendants. Sixteen cases (64%) rendered a defendant verdict, 6 (24%) favored the plaintiff, and 3 (12%) settled outside of court. Common allegations were poor cosmetic result (80%), negligence (68%), permanent injury (64%), and deficits of informed consent (60%). Emotional or psychological injury was alleged in 44% of cases.

Protecting Yourself

A higher proportion of cases resulted in payment when allegations of poor cosmetic outcome, negligence, inadequate consent, and inappropriate/unnecessary procedures were raised. These factors highlight the importance of exploring patient expectations. The consultation should include discussion of potential need for repeat treatment or further therapy if dissatisfied with results. Patients must understand postprocedure care and be counseled on warning signs of impending infection, acneiform reactions, and scarring for early intervention.

Perceived deficits in informed consent were alleged in 60%. Risks discussed should be carefully documented; unique consent forms outlining potential AEs for each procedure may be valuable for defending litigation.

Delegation of chemical peels and dermabrasion to nonphysicians requires appropriate supervision and training. Multiple studies demonstrate increasing complications from cosmetic procedures performed by nonphysicians in medical spas.[40–42] Moreover, there is significant variation in medical directorship and oversight among medical spas,[43,44] and only about 40% are overseen by a dermatologist or plastic surgeon.[44] Dermatologists are less likely than nondermatologist physicians to delegate cosmetic procedures.[45] Due to state-by-state variation, it is important to be sure nonphysicians may perform cosmetic procedures.[40] The state Board of Medical Examiners may provide this information.

TABLE 3. Chemical Peels and Dermabrasion Litigation Decided in Favor of Plaintiff[39]

Case	Sex	Defendant	Laser	Alleged Complication	Inadequate Informed Consent	Award* (Thousands, $)
1	F	Plastic surgeon	Chemical peel (TCA)	Infection, wound breakdown	No	724
2	F	Plastic surgeon	Chemical peel	Inability to close eyes, pain	No	453
3	F	Otolaryngologist	Dermabrasion	For rosacea, did not agree to dermabrasion	Yes	2,160
4	F	Plastic surgeon and aesthetician	Chemical peel (TCA)	Depigmentation	Yes	617
5	F	Plastic surgeon	Chemical peel (phenol)	Scars under eyes, numerous revisions	Yes	212
6	F	Primary care physician and aesthetician	Chemical peel (TCA) + dermabrasion	Acneiform reaction, scarring	Yes	62

* Award amounts in the article were adjusted for inflation in 2013.
F, female; TCA, trichloroacetic acid.

Sclerotherapy

Litigation

Sclerotherapy is a common, minimally invasive technique for removal of superficial veins.[46] Complication rates are exceedingly low, with hyperpigmentation and telangiectatic matting being common AEs.[47] Cutaneous necrosis is relatively rare and often self-limited; potentially major complications include arterial injection, anaphylaxis, nerve damage, thrombosis, and pulmonary embolus.[46]

To date, no studies of litigation involving sclerotherapy in the United States have been conducted. Dickhoff and colleagues[48] identified 23 medical liability insurance claims in the Netherlands arising after sclerotherapy. Skin necrosis due to inadvertent intra-arteriolar injection or reflex vasospasm from using too strong a solution was a common complication leading to litigation (17 cases); however, only 2 of these were ruled in favor of the plaintiff.

Protecting Yourself

While surgical and endovenous treatment of varicose veins can have significant complications, less invasive sclerotherapy is not without risk. Although US data are lacking, these may be learnt from colleagues in the Netherlands. Cutaneous necrosis was a leading cause of malpractice litigation after sclerotherapy. The most common cause of cutaneous necrosis is extravasation of sclerosant or injection into an unseen arteriole.[49] Strategies to avoid cutaneous necrosis include choice of sclerosant, knowledge of appropriate technique, stopping if blanching or a bleb forms, and utilizing proper compression.

Summary

Major causes for litigation among MICP and proposed risk mitigation strategies are summarized in the **Supplemental Digital Content 2** (See Table S1, http://links.lww.com/DSS/A890). Overall, dermatologists rank among the least likely physicians to face a malpractice claim.[7] Improper performance of a procedure, failure to supervise NPOs, and failure to recognize a complication are among the top medical errors resulting in litigation among all dermatology claims,[50] echoing themes observed for litigation in MICP. Providers of cosmetic procedures, however, are more likely to experience litigation than most other specialists; possible explanations include unrealistic patient expectations, aggressive malpractice lawyers, and inadequate pretreatment assessment. Recognizing malpractice trends is important to establish safeguards for patient care and minimize liability. General strategies to reduce risks of malpractice litigation in dermatology have been previously summarized.[50–52]

Limitations and Future Direction

Legal research databases, including Westlaw and LexisNexis, have several limitations. Most civil litigation is settled outside of court and not included. Likewise, complaints handled outside the judicial system (i.e., third-party arbitration) are not included. These databases fail to detect cases filed in small claims courts or frivolous claims with little merit. Finally, data submission requirements vary by jurisdiction. While limited by their breadth and inability to estimate the incidence of litigation, these databases help identify key allegations and their outcomes.

Alternate resources, such as the Physician Insurers Association of America, may help capture malpractice claims data among procedures not discussed here. Future studies should evaluate other common cosmetic procedures, including hair transplantation and body contouring devices. Meanwhile, the FDA Manufacturer and User Facility Device Experience database provides insight on AEs to be aware of and appropriately counsel patients during

consultation.[13,46,53–56] Improved reporting of complications for physicians and nonphysicians may identify additional strategies to improve patient care and ultimately reduce malpractice lawsuits.

The recommendations (See **Supplemental Digital Content 1**, Table S1, http://links.lww.com/DSS/A890) are based on an overall low case total and represent the author's suggestions based on the interpretation of the literature and individual case law. These guidelines are written from a US perspective.[22,31,57–68] It is important to know your own state and local laws, and when in doubt, consult an attorney for more information.

Conclusion

Various medicolegal issues can arise from the practice of cosmetic medicine. Reviewing malpractice litigation for MICP highlights multiple recurring themes. Careful patient selection, pretreatment evaluation, fully informed consent, proper training and oversight of procedures, and ensuring patient compliance with postprocedure care and follow-up are critical to minimize risks. Providers must know local laws and regulations regarding delegation of procedures, for they may be vicariously liable for the actions of their employees. Nonphysicians and physicians without specific training in cosmetic procedures are held to the same standard of care expected of physicians trained in delivering these treatments. Understanding malpractice trends and reasons for litigation in MICP can strengthen the patient–provider relationship and offer strategies to minimize risk of a lawsuit.

References

1. American Society for Dermatology Surgery. ASDS Survey on Dermatologic Procedures. Available from: https://www.asds.net/Portals/0/Images/body-procedures-survey-results-infographic-2018.jpg. Accessed May 6, 2020.
2. Bangash HK, Eisen DB, Armstrong AW, Nelson AA, et al. Who are the pioneers? A critical analysis of innovation and expertise in cutaneous noninvasive and minimally invasive cosmetic and surgical procedures. *Dermatol Surg* 2016;42:335–51.
3. Ahn CS, Davis SA, Dabade TS, Williford PM, et al. Cosmetic procedures performed in the United States: a 16-year analysis. *Dermatol Surg* 2013;39:1351–9.
4. Jalian HR, Jalian CA, Avram MM. Common causes of injury and legal action in laser surgery. *JAMA Dermatol* 2013;149:188–93.
5. Paik AM, Mady LJ, Sood A, Lee ES. Beyond the operating room: a look at legal liability in body contouring procedures. *Aesthet Surg J* 2014;34:106–13.
6. Halepas S, Lee KC, Higham ZL, Ferneini EM. A 20-year analysis of adverse events and litigation with light-based skin resurfacing procedures. *J Oral Maxillofac Surg* 2020;78:619–28.
7. Jena AB, Chandra A, Lakdawalla D, Seabury S. Outcomes of medical malpractice litigation against US physicians. *Arch Intern Med* 2012;172:892–4.
8. Hibler BP, Avram M. Protecting yourself: legal issues in aesthetic medicine—informed consent, discharge, & lawsuits. In: Rieder E, Fried R, editors. *Essential Psychiatry for the Aesthetic Practitioner*. West Sussex, United Kingdom: Wiley Blackwell; 2021. ISBN 978-1-119-68006-2.
9. Mejia NI, Vuong KD, Jankovic J. Long-term botulinum toxin efficacy, safety, and immunogenicity. *Mov Disord* 2005;20:592–7.
10. Coté TR, Mohan AK, Polder JA, Walton MK, et al. Botulinum toxin type A injections: adverse events reported to the US food and drug administration in therapeutic and cosmetic cases. *J Am Acad Dermatol* 2005;53:407–15.
11. Korman JB, Jalian HR, Avram MM. Analysis of botulinum toxin products and litigation in the United States. *Dermatol Surg* 2013;39:1587–91.
12. Ezra N, Peacock EA, Keele BJ, Kingsley M. Litigation arising from the use of soft-tissue fillers in the United States. *J Am Acad Dermatol* 2015;73:702–4.
13. Ortiz AE, Ahluwalia J, Song SS, Avram MM. Analysis of US food and drug administration data on soft-tissue filler complications. *Dermatol Surg* 2020;46:958–61.
14. Rayess HM, Svider PF, Hanba C, Patel VS, et al. A cross-sectional analysis of adverse events and litigation for injectable fillers. *JAMA Facial Plast Surg* 2018;20:207–14.
15. Beauvais D, Ferneini EM. Complications and litigation associated with injectable facial fillers: a cross-sectional study. *J Oral Maxillofac Surg* 2020;78:133–40.
16. Ferneini EM, Hapelas S, Watras J, Ferneini AM, et al. Surgeon's guide to facial soft tissue filler injections: relevant anatomy and safety considerations. *J Oral Maxillofac Surg* 2017;75:2667.e1–67.e5.
17. Cohen JL. Understanding, avoiding, and managing dermal filler complications. *Dermatol Surg* 2008;34(Suppl 1):S92–9.
18. Goldberg DJ. Medical-legal considerations in the medical spa environment. *Dermatol Clin* 2008;26:387–90, vi.
19. Anderson RR. Lasers for dermatology and skin biology. *J Invest Dermatol* 2013;133:E21–3.
20. Jalian HR, Jalian CA, Avram MM. Increased risk of litigation associated with laser surgery by nonphysician operators. *JAMA Dermatol* 2014;150:407–11.
21. Pierce RR, Martell DW. Ablative lasers: 24 years of medical malpractice cases in the United States. *Dermatol Surg* 2018;44:730–1.
22. Svider PF, Carron MA, Zuliani GF, Eloy JA, et al. Lasers and losers in the eyes of the law: liability for head and neck procedures. *JAMA Facial Plast Surg* 2014;16:277–83.
23. Daggett C, Daggett A, McBurney E, Murina A. Laser safety: the need for protocols. *Cutis* 2020;106:87–92.
24. DiGiorgio CM, Avram MM. Laws and regulations of laser operation in the United States. *Lasers Surg Med* 2018;50:272–9.
25. American Society for Dermatologic Surgery Association. American Society for Dermatologic Surgery Association Position on the Practice of Medicine and the Delegation of Medical Procedures to Allied Health Professionals. Available from: http://asdsa.asds.net/training-and-delegation.aspx. Accessed May 7, 2021.
26. American Society for Dermatologic Surgery Association. Position on Use of Dermal Fillers and Injectables. Available from: https://www.asds.net/Portals/0/PDF/ASDS-Use-of-Dermal-Fillers-and-Injectables.pdf. Accessed May 7, 2021.
27. Hammes S, Karsai S, Metelmann HR, Pohl L, et al. Treatment errors resulting from use of lasers and IPL by medical laypersons: results of a nationwide survey. *J Dtsch Dermatol Ges* 2013;11:149–56.
28. Coleman WP III, Hanke CW, Lillis P, Bernstein G, et al. Does the location of the surgery or the specialty of the physician affect malpractice claims in liposuction? *Dermatol Surg* 1999;25:343–7.
29. Therattil PJ, Chung S, Sood A, Granick MS, et al. An analysis of malpractice litigation and expert witnesses in plastic surgery. *Eplasty* 2017;17:e30.
30. Svider PF, Keeley BR, Zumba O, Mauro AC, et al. From the operating room to the courtroom: a comprehensive characterization of litigation related to facial plastic surgery procedures. *Laryngoscope* 2013;123:1849–53.
31. Bismark MM, Gogos AJ, McCombe D, Clark RB, et al. Legal disputes over informed consent for cosmetic procedures: a descriptive study of negligence claims and complaints in Australia. *J Plast Reconstr Aesthet Surg* 2012;65:1506–12.
32. Park BY, Kwon J, Kang SR, Hong SE. Informed consent as a litigation strategy in the field of aesthetic surgery: an analysis based on court precedents. *Arch Plast Surg* 2016;43:402–10.
33. Klein JA. The tumescent technique. Anesthesia and modified liposuction technique. *Dermatol Clin* 1990;8:425–37.

34. Samdal F, Amland PF, Bugge JF. Blood loss during liposuction using the tumescent technique. *Aesthetic Plast Surg* 1994;18:157–60.
35. Klein JA. Tumescent technique for local anesthesia improves safety in large-volume liposuction. *Plast Reconstr Surg* 1993;92:1085–98; discussion 99–100.
36. Halk AB, Habbema L, Genders RE, Hanke CW. Safety studies in the field of liposuction: a systematic review. *Dermatol Surg* 2019;45: 171–82.
37. Coleman WP III, Coleman JG. Liposuction and the law. *Dermatol Clin* 1990;8:569–80.
38. Svedman KJ, Coldiron B, Coleman WP III, Cox SE, et al. ASDS guidelines of care for tumescent liposuction. *Dermatol Surg* 2006;32: 709–16.
39. Svider PF, Jiron J, Zuliani G, Shkoukani MA, et al. Unattractive consequences: litigation from facial dermabrasion and chemical peels. *Aesthet Surg J* 2014;34:1244–9.
40. Brody HJ, Geronemus RG, Farris PK. Beauty versus medicine: the nonphysician practice of dermatologic surgery. *Dermatol Surg* 2003; 29:319–24.
41. Rossi AM, Wilson B, Hibler BP, Drake LA. Nonphysician practice of cosmetic dermatology: a patient and physician perspective of outcomes and adverse events. *Dermatol Surg* 2019;45:588–97.
42. Wang JV, Albornoz CA, Goldbach H, Mesinkovska N, et al. Experiences with medical spas and associated complications: a survey of aesthetic practitioners. *Dermatol Surg* 2020;46:1543–8.
43. Walgrave S, Jacobs MA, Kist D, Weaver AL, et al. Survey of regional laser centers: a Minnesota perspective. *Dermatol Surg* 2011;37: 612–8.
44. Gibson JF, Srivastava D, Nijhawan RI. Medical oversight and scope of practice of medical spas (Med-Spas). *Dermatol Surg* 2019;45:581–7.
45. Austin MB, Srivastava D, Bernstein IH, Dover JS. A survey comparing delegation of cosmetic procedures between dermatologists and nondermatologists. *Dermatol Surg* 2015;41:827–32.
46. Weiss MA, Hsu JT, Neuhaus I, Sadick NS, et al. Consensus for sclerotherapy. *Dermatol Surg* 2014;40:1309–18.
47. Goldman MP, Sadick NS, Weiss RA. Cutaneous necrosis, telangiectatic matting, and hyperpigmentation following sclerotherapy. Etiology, prevention, and treatment. *Dermatol Surg* 1995;21:19–29; quiz 31–2.
48. Dickhoff C, Cremers JE, Legemate DA, Koelemay MJ. Medical liability insurance claims after treatment of varicose veins. *Phlebology* 2014;29:293–7.
49. Bergan JJ, Weiss RA, Goldman MP. Extensive tissue necrosis following high-concentration sclerotherapy for varicose veins. *Dermatol Surg* 2000;26:535–41; discussion 41–2.
50. Kornmehl H, Singh S, Adler BL, Wolf AE, et al. Characteristics of medical liability claims against dermatologists from 1991 through 2015. *JAMA Dermatol* 2018;154:160–6.
51. Shah VV, Kapp MB, Wolverton SE. Medical malpractice in dermatology. Part I: reducing the risks of a lawsuit. *Am J Clin Dermatol* 2016;17:593–600.
52. Shah VV, Kapp MB, Wolverton SE. Medical malpractice in dermatology. Part II: what to do once you have been served with a lawsuit. *Am J Clin Dermatol* 2016;17:601–7.
53. Tremaine AM, Avram MM. FDA MAUDE data on complications with lasers, light sources, and energy-based devices. *Lasers Surg Med* 2015;47:133–40.
54. Nadimi S. Complications with hair transplantation. *Facial Plast Surg Clin North Am* 2020;28:225–35.
55. Vanaman M, Fabi SG, Carruthers J. Complications in the cosmetic dermatology patient: a review and our experience (part 1). *Dermatol Surg* 2016;42:1–11.
56. Vanaman M, Fabi SG, Carruthers J. Complications in the cosmetic dermatology patient: a review and our experience (part 2). *Dermatol Surg* 2016;42:12–20.
57. Mavroforou A, Giannoukas A, Michalodimitrakis E. Medical litigation in cosmetic plastic surgery. *Med Law* 2004;23:479–88.
58. Sacchidanand SA, Bhat S. Safe practice of cosmetic dermatology: avoiding legal tangles. *J Cutan Aesthet Surg* 2012;5:170–5.
59. Kalter PO, van der Baan B, Vuyk H. Medicolegal aspects of otolaryngologic, facial plastic, and reconstructive surgery. *Facial Plast Surg* 1995;11:105–10.
60. Shinal v. Toms, 162 A.3d 429 (Pa. 2017).
61. Sawicki N. IRBs Advise Physician Involvement in Informed Consent. Available from: https://blog.petrieflom.law.harvard.edu/2017/09/13/irbs-advise-physician-involvement-in-informed-consent/. Accessed May 17, 2020.
62. Fernandez Lynch H, Joffe S, Feldman EA. Informed consent and the role of the treating physician. *N Engl J Med* 2018;379:e25.
63. *Baribeau v. Gustafson, Texas Court of Appeals (Bexar County). Case No. 04-01-000732-CV (2002).*
64. Makdessian AS, Ellis DA, Irish JC. Informed consent in facial plastic surgery: effectiveness of a simple educational intervention. *Arch Facial Plast Surg* 2004;6:26–30.
65. Paik AM, Mady LJ, Sood A, Eloy JA, et al. A look inside the courtroom: an analysis of 292 cosmetic breast surgery medical malpractice cases. *Aesthet Surg J* 2014;34:79–86.
66. *Miller v. Kennedy, 11 Wn. App. 272 (Wash. Ct. App. 1974).*
67. Sweis IE, Spitz J, Barry DR Jr, Cohen M. A review of body dysmorphic disorder in aesthetic surgery patients and the legal implications. *Aesthetic Plast Surg* 2017;41:949–54.
68. Shiffman MA. Medical liability issues in cosmetic and plastic surgery. *Med Law* 2005;24:211–32.

Original Article

Midlevel Injectable Practice Patterns in Dermatology and Plastic Surgery Offices

Lauren Nesi, BS, Matthew Belcher, MD, Ashley Decker, MD, and Naomi Lawrence, MD*

BACKGROUND There is limited knowledge on the extent physicians delegate cosmetic procedures to midlevel providers.

OBJECTIVE To assess dermatology and plastic surgery practice patterns for the injections of neurotoxins and dermal fillers.

MATERIALS AND METHODS Four hundred ninety-two dermatology and plastic surgery practices were identified from 10 major US metropolitan areas. These practices were contacted, and staff were asked a series of questions to best characterize the practice patterns in regard to who performs the injectables in the office.

RESULTS Although most dermatology and plastic surgery practices had physicians as the only provider who gives injectables, 18.35% of dermatology and 25.4% of plastic surgery practices had nurse practioners and physician assistants giving injectables both with and without oversight of the supervising physician onsite.

CONCLUSION In a large majority of both plastic surgery and dermatology practices, physicians exclusively perform injections of neurotoxins and fillers. For practices that allow midlevel providers to perform injectables, the level of physician supervision is variable. In a small percentage of plastic surgery practices, surveyed midlevel providers exclusively performed injectables.

In recent decades, the use of cosmetic soft tissue injectables and neurotoxins has risen dramatically, with more than 15 million minimally invasive procedures performed in 2018.[1] The increased popularity of injectables is due to excellent and reproducible aesthetic results with limited-to-no recovery time. Although these procedures have an excellent safety profile, they are not risk free. The use of soft tissue modulators has a small but significant risk of cutaneous necrosis and permanent blindness, whereas neuromodulators placed incorrectly can result in ptosis, asymmetry, and functional defects of the eyelid lasting for months.[2] It is imperative that injectors understand the different characteristics of each type of filler, risks of complications, injection techniques, and management of patients who experience adverse events.[3] Urgent interventions by knowledgeable providers can restore blood flow after vascular compromise due to filler injection. Relief of ischemia due to retinal artery occlusion may require advanced techniques, such as retrobulbar injection of hyaluronidase by physicians.[2]

Previous studies have shown that midlevel providers are being increasingly used in the delivery of dermatologic care. The term "midlevel practitioners" is defined by the US Drug Enforcement Administration as an "individual practitioner, other than a physician, dentist, veterinarian, or podiatrist, who is licensed, registered, or otherwise permitted by the United States or the jurisdiction in which he/she practices, to dispense a controlled substance in the course of professional practice. Examples of midlevel practitioners include, but are not limited to, health care providers such as nurse practitioners, nurse midwives, nurse anesthetists, clinical nurse specialists, and physician assistants who are authorized to dispense controlled substances by the state in which they practice."[4] Although nurse practitioner (NP) and physician's assistant (PA) roles evolved at first to meet the rising needs in primary care, they later expanded to specialties in medicine, including dermatology.[5] The number of individuals becoming NPs and PAs is rising each year; the US Bureau of Labor Statistics predicts a 37% increase in employment for PAs and a 31% increase in employment for NPs from 2016 to 2026.[6,7] They provide a cost-efficient supply of hands-on care previously provided by physicians.[4] Although PAs, NPs, and board-certified physicians all perform cosmetic procedures, there is a discrepancy between the length of education training and hours of training. Board-certified dermatologists have a minimum of 8 years of graduate medical education and between 12,000 to 16,000 hours of patient care. Physician's assistants have 2 to 3 years of graduate education with 2000 required hours of patient care. Finally, NPs have 2 to 4 years of graduate education, depending on if they get a masters or doctoral degree with 500 to 720 hours requirements.[8] Because of the discrepancy in the length of training and rigor of didactics, medical practices traditionally have physician-led, team-based care. Physicians maintain authority for patient care in this team-based approach to guarantee patient safety and quality of care.

*From the *All authors are affiliated with the Department of Dermatological Surgery, Cooper University Health Care, Camden, New Jersey*

The authors have indicated no significant interest with commercial supporters.

Address correspondence and reprint requests to: Naomi Lawrence, MD, 10000 Sagemore Dr #10103, Marlton, NJ 08053, or e-mail: lawrence-naomi@cooperhealth.edu

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.dermatologicsurgery.org).

http://dx.doi.org/10.1097/DSS.0000000000002927

Although advanced practice nurses (APNs) and PAs are certified nationally, state laws actually determine the specific level of care allowed by midlevel providers.[9] Specifically, they determine the level of education needed, the amount of prescriptive authority allowed, and the amount of physician involvement required. Although some states have detailed legislation, many states have open-ended and ambiguous legislation.[10] The state scope-of-practice laws place limits on the clinical boundaries advanced practioners must abide by.[10] The American Medical Association (AMA) strongly supports these scope-of-practice laws as necessary to ensure patient safety and best practice.[10] Legally, NPs and PAs are allowed to give injectables, with physician oversight. The interpretation of what "physician oversight" entails and whether physicians need to be physically on the premises is not detailed in federal laws. As a result, the level of care allowed by midlevel providers is open to the interpretation of each supervising physician.

Although it is known that some physicians delegate cosmetic procedures to midlevel providers, no studies exist to determine current practice patterns. In this study, we sought to identify the individual practice patterns for the injections of neurotoxins and fillers for dermatologist and plastic surgeons. Specifically, we wanted to identify which provider within these practices is performing these treatments (midlevel providers vs dermatologists/plastic surgeons). We hypothesize that although most dermatologists and plastic surgeons perform injections themselves, there is still a minority delegating these procedures to midlevel providers. This will allow for an improved understanding of how cosmetic procedures are delegated and help providers determine practice standards when deciding who in their office should perform cosmetic procedures.

Materials and Methods

Study Design

Our study design centered on telephone calls to offices of dermatologists and plastic surgeons in the largest US metropolitan areas. Calls involved a series of questions to determine if cosmetic injectable procedures were offered for patients and if offered, who performed the procedure (MD, NP, PA, or others).

Each practice was assigned a number, and the answers to the above questions were recorded. Neither the names of the practices nor the practicing physicians were recorded. The answers to the questions and the type of practice were recorded.

A different researcher then analyzed the data, with all practices and physician's deidentified, to determine the percentage of offices that offer injectable procedures and have injectable procedures performed by physicians versus nonphysician providers.

Number of Subjects

In this study, we identified dermatology and plastic surgery practices located within 11 major US metropolitan areas using the American Academy of Dermatology and American Society of Plastic Surgeons Web sites. The cities included were New York, Chicago, Boston, Philadelphia, Washington D.C., Atlanta, Dallas, Houston, Los Angeles, San Francisco, and Miami. In total, 492 dermatology and plastic surgeon practices were queried. Practices located outside of major city limits were excluded. In addition, several practices were excluded because of incorrectly listed phone numbers and front desk staff who were unable to answer questions.

Procedure

A trained member of our staff called the offices using contact information provided on the professional organization Web sites (American Academy of Dermatology and American Society of Plastic Surgeons) and asked a series of questions: (1) Does their practice offer injectables? (2) Are the injections performed by an MD, PA, NP, or other providers? (3) If a nonphysician typically performs the injections, is an MD available to inject on request? (4) If an MD performs the initial injection, will they also perform the injections at follow-up visits? and (5) If a nonphysician performs injections, is a physician on-site? The answers were then recorded on a data recording sheet with no identifiable information to prevent any association of answers with the practices that gave them. The list of practices (identified through professional organizations) was also kept separate from the data recording sheet (See **Supplemental Digital Content 1**, Table S1, http://links.lww.com/DSS/A658).

Statistical Analysis

The data were analyzed by a physician investigator who did not perform the initial data collection to determine the percent of practices in which MDs or other providers perform injectables in these scenarios. Data analysis was performed using Microsoft Excel (Microsoft Corporation, Redmond, WA).

Results

Of the 250 dermatology and 582 plastic surgery practices identified, 117 dermatology and 373 plastic surgery practices met inclusion criteria. Of those, an additional 8 dermatology practices were excluded, and 23 plastic surgery practices were excluded because these practices did not offer injections of neurotoxins or dermal fillers. Of the dermatology practices identified, 81.7% reported that the physician was the only individual to perform the injections, whereas 74.6% of plastic surgery offices reported that the physician was the only individual to perform the injections (Table 1). Consequently, 18.4% of dermatology practices offering injectables answered to having midlevels performing injectables and 20.3% of plastic surgery offices have midlevels performing injectables. Of the practices surveyed, 0% dermatology practices and 5.1% of plastic surgeons had no MD oversight, with only midlevels performing injections.

TABLE 1. Survey Results

Dermatology Practices	Response Number	Percent
Doctor only	89	81.65
Multiple providers	20	18.35
No injections offered	8	
Plastic Surgery Practices	**Response Number**	**Percent**
Doctor only	261	73.6
Multiple providers	71	20.3
No injections offered	23	
No physician at practice	18	5.1

Of the 20 dermatology practices with midlevel injectors, 2 practices confirmed that a physician was onsite at all times, whereas of the 71 total plastic surgery offices with midlevel injectors, 26 confirmed that a physician was onsite at all times. The other midlevel injectable practices had varying responses that included: never, not always, or did not know the office policy on midlevel injectable physician supervision. Many offices also responded that the supervising physicians were in a separate building or separate floor.

Discussion

The role of midlevel practitioners in dermatology and plastic surgery practices is controversial and highly debated. However, studies have shown that midlevel providers are being increasingly used in the delivery of dermatological care. Little knowledge exists on what the breakdown is for types of health care professionals delivering cosmetic procedures in the United States. There are no current studies identifying practice patterns.

This study identified practice patterns and norms, which is informative to both patients seeking cosmetic treatments as well as physicians delegating procedures within their offices. A large majority of both dermatology practices (81.7%) and plastic surgery practices (74.6%) use only physicians in the delivery of cosmetic injectables. Although most of both dermatologists and plastic surgeons are still the main provider of injectables in their respective practices, approximately 20% of both dermatology and plastic surgery practices also used midlevel providers for injectable neurotoxins and fillers. 5.1% of surveyed plastic surgery practices used midlevel providers exclusively for injectables. This evidence suggests that there is an expanded role of midlevel providers on a national level.

As NPs and PAs define their role in this shifting environment, concerns about their effectiveness and use are often brought up. A 2015 study by Nault and colleagues showed that the number of biopsies required to find a malignancy was twice as high for advanced practice professionals (APPs) as compared to dermatologists. Consequently, this study concluded that the use of APPs increased morbidity and cost of care compared with a board-certified dermatologist.[11] By contrast, a study in JAMA from 2000 found no significant difference in primary care outcomes primary care physicians and NPs.[12] Evidence from other studies confirm primary care services such as the management of uncomplicated illness and chronic disease can be provided by NPs at least as effectively as physicians.[13]

The utility of midlevels in a primary care capacity has been widely accepted; however, the capacity in which they practice is widely variable. The scope-of-practice laws are state-specific restrictions that determine what tasks midlevel practioners may undertake while treating patients. Each state has different regulations for the scope-of-practice of NPs and PAs.[14] There is variation in prescribing privileges, oversight and chart reviews, and the maximum "collaboration ratios" for NPs working with physicians.[13] Sixteen states and the District of Columbia had standardized their scope-of-practice regulations and allow NPs to practice and prescribe independently.[13]

With the growing use of nonsurgical aesthetic procedures across the country, practices have adapted to meet this growing demand from consumers.[1] Physicians continue to delegate these procedures to nonphysician providers with supervision, depending on their individual state's scope-of-practice.[15] Presently, there are no specialty boards that regulate the practice of these providers.[15] One of the key concerns is the lack of a common method taught to these midlevel providers guiding midlevel practioners on the use of dermal fillers and injectables. A study in Plastic Surgery Nursing surveyed 103 nursing providers and found that there were common core deficits in respondents' knowledge of contradictions for the use of injectables and management of postprocedure complications.[15] Most respondents of this survey performing a minimum of 10 procedures under physician supervision before practicing independently, whereas 12.5% of the respondents reported more than 20. It is essential that competencies are developed to assess and evaluate the quality of current practice to ensure safe treatments.

We were surprised to see that a significant number of practices that use midlevel injectors could not verify on-site supervision at all times. As described above, there are risks of temporary and permanent side effects from improper techniques. Different injectables have a wide range of properties and associated adverse events. The injector needs to be sufficiently experienced with the products being used, maintain a detailed understanding of facial anatomy, and be prepared to provide appropriate treatment in the case of adverse events. The ultimate responsibility for each patient's outcome rests on solely on the supervising physician. For

optimal results, physician oversight is essential to providing high-quality injectables.

This study had several limitations. First, individual practice information was restricted to the knowledge of the office staff who provided the responses that would limit the accuracy of responses. Responses may also be biased with staff more likely to overstate the degree to which physicians perform injections and deemphasize the amount of injections delegated to nonphysicians. In addition, the sequence of questions asked may lead to skewed responses for respondents. Many physicians have multiple offices with various ways that injections are performed which may not be accurately assessed by our survey, although it was requested for respondents to include answers for their offices. Another limitation is that this study only examined practices within the 10 major cities. The generalizability of our results is limited to practices that fall within metropolitan areas. It is possible that there is a difference between practice patterns between suburban and rural groups. Future studies may examine if there is a difference between these environments.

One of the national concerns has been the change in practice model created by the introduction of private equity backed conglomerate practices. These business investments made by private equity groups have a profit-centered focus. Financial analysts and businessmen are dictating how doctors practice to make the highest profit. The use of midlevels rather than board-certified physicians saves costs leading to higher profits. Private equity groups made up 30% of the dermatology practices using midlevel providers (n = 6), whereas nationally, only 16% of dermatology practices belong to private equity groups.[16] Because of the low sample size, these data were not included in our initial analysis. Future studies might further examine the private equity group use of midlevel injectors on a national level compared with academic institutions.

References

1. Statistics ANCoPSP. *2018 Plastic Surgery Statistics Report*. 2018.
2. Carruthers JC. *Soft Tissue Augmentation*. Alam JD, editor. Amsterdam, the Netherland: Elsevier; 2018; pp. 236.
3. Funt D, Pavicic T. Dermal fillers in aesthetics: an overview of adverse events and treatment approaches. *Clin Cosmet Investig Dermatol* 2013;6:295.
4. Administration DE. *Mid-Level Practitioner Authorization by State: Department of Justice*. 1993. Available from: https://www.deadiversion.usdoj.gov/drugreg/practioners/mlp_by_state.pdf.
5. Cooper RA. New directions for nurse practitioners and physician assistants in the era of physician shortages. *Acad Med* 2007;82:827–8.
6. United States Department of Labor BoLS. *Occupational Outlook Handbook, Nurse Anesthetists, Nurse Midwives, and Nurse Practitioners*. Available from: https://www.bls.gov/ooh/healthcare/nurse-anesthetists-nurse-midwives-and-nurse-practitioners.htm.
7. United States Department of Labor BoLS. *Occupational Outlook Handbook, Healthcare, Physician Assistants*. Available from: https://www.bls.gov/ooh/healthcare/physician-assistants.htm. Accessed June 18, 2019.
8. Dermatology AAo. Why see a board certified dermatologist? American Academy of Dermatology. 2019. Available from: https://www.aad.org/public/diseases/why-see-a-board-certified-dermatologist#texteducation.
9. Gadbois EA, Miller EA, Tyler D, Intrator O. Trends in state regulation of nurse practitioners and physician assistants, 2001 to 2010. *Med Care Res Rev* 2015;72:200–19.
10. Cooper RA. Health care workforce for the twenty-first century: the impact of nonphysician clinicians. *Annu Rev Med* 2001;52:51–61.
11. Nault A, Zhang C, Kim K, Saha S, et al. Biopsy use in skin cancer diagnosis: comparing dermatology physicians and advanced practice professionals. *JAMA Dermatol* 2015;151:899–902.
12. Mundinger MO, Kane RL, Lenz ER, Totten AM, et al. Primary care outcomes in patients treated by nurse practitioners or physicians: a randomized trial. *JAMA* 2000;283:59–68.
13. Fairman JA, Rowe JW, Hassmiller S, Shalala DE. Broadening the scope of nursing practice. *J Dermatol Nurses Assoc* 2011;3:88–90.
14. Timmons EJ. The effects of expanded nurse practitioner and physician assistant scope of practice on the cost of Medicaid patient care. *Health Policy* 2017;121:189–96.
15. What are the necessary practice competencies for two providers: dermal fillers and botulism toxin type a injections. *Plast Surg Nurs* 2010;30:226–46.
16. Association AAoD. *Pulling Back the Curtain on Private Equity*. Vol 28. Des Plaines, IL: Dermatology World; 2018.

Millennial Perspectives on Body-Contouring Procedures: A National Survey

Body-contouring procedures have experienced a fourfold increase in popularity over the past 7 years.[1] High body dissatisfaction rates associated with sedentary lifestyles and unbalanced diets continue to fuel the demand for fat reduction and body contouring. In addition, these procedures have also become popular with younger consumers, who have continued to seek out minimally and noninvasive cosmetic treatments. In 2018, 20.2% of nonsurgical fat reduction procedures were performed in patients who were 18 to 34 years old.[2] With Millennials representing a growing share of aesthetic patients, we decided to evaluate their perspectives on noninvasive body contouring procedures to offer practitioners a better understanding of their views and opinions.

An online survey was distributed to individual consumers in the United States who were 24 to 39 years old in March 2020. The survey included demographic data as well as experiences with and attitudes to noninvasive body contouring procedures. Top-box scoring was used to evaluate questions using the Likert scale.

A total of 116 respondents completed the survey. The mean age was 32.0 years, and 55.2% were women. Of all respondents, 26.7% had a previous cosmetic procedure, of which 35.5% will have another in the future. Overall, 16.4% are currently planning to have a future procedure, and 48.3% are considering it.

Respondents had varying degrees of knowledge about body contouring procedures (see **Supplemental Digital Content 1**, Figure S1, http://links.lww.com/DSS/A518). They generally believed them to be effective to different extents (Figure 1). Significantly more respondents believed them to be effective when they or someone they knew had the procedure performed (71.7% vs 48.2%; $p = .010$). The majority (63.8%) were also interested in learning more about body contouring.

Of all respondents, 16.4% underwent a body-contouring procedure, and 40.5% knew of others who had it performed. Interestingly, most procedures were performed in the medical spa setting as opposed to a physician practice for both respondents themselves (78.9% vs 36.8%; $p = .009$) and people they knew (76.6% vs 59.6%; $p = .078$). Of the 38.8% who were certainly interested in having a body-contouring procedure performed, the majority (75.6%) preferred a medical spa setting. By contrast, of the 34.5% who were possibly considering the procedure, there was instead a greater preference for a physician practice (67.5%). A slight majority believed that medical spas were similar to physician-based practices in terms of safety (59.5%) and outcomes (63.8%) for body contouring procedures.

When selecting a clinic or practitioner, many sources of information are used (see **Supplemental Digital Content 2**, Figure S2, http://links.lww.com/DSS/A519). When deciding between a medical spa and physician practice, respondents have many considerations (see **Supplemental Digital Content 3**, Figure S3, http://links.lww.com/DSS/A520). Interestingly, the vast majority (90.5%) will check the

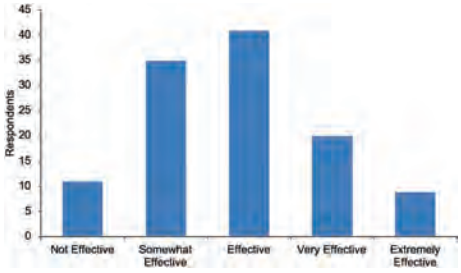


Figure 1. Perceived effectiveness of body contouring procedures by respondents.

ISSN: 1076-0512 • Dermatol Surg 2020;00:1–3 •

ATTACHMENT D

level of training and credentials of a medical spa practitioner before undergoing a procedure. More respondents believed physician practices were trustworthy compared to medical spas (77.6% vs 61.2%; $p = .007$).

The rising demand for noninvasive body contouring is largely driven by a desire to avoid more invasive procedures and their associated downtime and risks. Liposuction is still considered the gold standard for fat removal and remains one of the most commonly performed aesthetic procedures worldwide. However, newer noninvasive body contouring techniques can offer an improved safety profile with limited downtime. Although the risks include postprocedural pain, swelling, and paradoxical adipocyte hyperplasia, the procedures are generally well tolerated, and there is no requirement for general anesthesia.

Current modalities allow for the safe and effective targeting of fat, and some also provide the added benefit of tissue tightening or muscle toning. These advanced methods of noninvasive lipolysis target fat cells by taking advantage of their physical properties that differentiate them from surrounding dermis and epidermis. Common treatments include cryolipolysis, radiofrequency, focused ultrasound, and laser energy. Electromagnetic muscle stimulation is one of the more recently developed therapies for body contouring, which specifically targets muscles by selectively stimulating motor neurons to induce tonic muscle contractions while simultaneously increasing fat metabolism.[3]

Given the rapidly evolving landscape of available treatment options, it is no wonder that so many respondents have limited knowledge on body-contouring procedures. However, greater familiarity with them, whether by first-hand or second-hand experience, significantly improved the opinions of their efficacy. Perhaps additional informative marketing and consumer education may expand consumer interest in body-contouring procedures while also maintaining accurate and realistic expectations.

Many respondents either already had or were interested in having body-contouring procedures performed in a medical spa setting. A slim majority also believed medical spas to be similar to physician practices in terms of safety and outcomes for these procedures. Interestingly, there was a preference for medical spas by those who were certainly interested in having a body-contouring procedure, but this preference switched to physician practices when respondents were still considering it. Perhaps those who remain cautious about undergoing cosmetic procedures prefer treatment in a true medical setting, especially because safety was cited as the top consideration when deciding between medical spas and physician practices.

Given the constant technologic advancements and increasing complexity behind the procedures, treatments may be better suited for physician-based practices as opposed to medical spas, which have recently been associated with patient complications due to deficiencies in training and supervision, improper technique, and incorrect device settings.[4] Fortunately, dermatologists are still the most frequently desired cosmetic provider, especially when compared to medical spas, aestheticians, and registered nurses.[5] Promoting awareness of the discrepancies between practice types may perhaps offer patients more perspective. Additional studies should further examine the differences in patient safety and outcomes between medical spas and physician practices to shed more light on this important topic.

The emerging popularity of body-contouring procedures shows no signs of slowing, and the demand is only expected to rise in coming years. With Millennials accounting for a growing share of aesthetic patients, it is crucial for practitioners to stay informed regarding shifts in consumer perspectives.

References

1. American Society for Dermatologic Surgery. *Survey on Dermatologic Procedures: Report of 2018 Procedures*. Available from: https://www.asds.net/portals/0/PDF/procedures-survey-results-presentation-2018.pdf. Accessed March 20, 2020.
2. The American Society for Aesthetic Plastic Surgery. *Cosmetic Surgery National Data Bank: Statistics 2018*. Available from: https://www.surgery.org/sites/default/files/ASAPS-Stats2018_0.pdf. Accessed May 14, 2020.

3. Jacob CI, Paskova K. Safety and efficacy of a novel high-intensity focused electromagnetic technology device for noninvasive abdominal body shaping. J Cosmet Dermatol 2018;17:783–7.

4. Wang JV, Albornoz CA, Goldbach H, Mesinkovska N, et al. Experiences with medical spas and associated complications: a survey of aesthetic practitioners. Dermatol Surg Epub 2020 Feb 11.

5. Wang JV, Zachary CB, Saedi N. Factors influencing consumer decisions in aesthetics: selection of procedures and practitioners. Dermatol Surg Epub 2020 Aug 6.

Jordan V. Wang, MD, MBE, MBA*
Robert D. Murgia, DO, MA†
Christian A. Albornoz, MD*
Nazanin Saedi, MD*

*Department of Dermatology and Cutaneous Biology
Thomas Jefferson University
Philadelphia, Pennsylvania
†Maryland Dermatology Laser
Skin, & Vein Institute
Hunt Valley, Maryland

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the full text and PDF versions of this article on the journal's Web site (www.dermatologicsurgery.org).

The authors have indicated no significant interest with commercial supporters.

ATTACHMENT D

Nonphysician Practice of Cosmetic Dermatology: A Patient and Physician Perspective of Outcomes and Adverse Events

Anthony M. Rossi, MD,* Britney Wilson, BA, MBS,* Brian P. Hibler, MD,* and Lynn A. Drake, MD†

BACKGROUND Nonphysicians are expanding practice into specialty medicine. There are limited studies on patient and physician perspectives as well as safety outcomes regarding the nonphysician practice of cosmetic procedures.

OBJECTIVE To identify the patient (consumer) and physician perspective on preferences, adverse events, and outcomes following cosmetic dermatology procedures performed by physicians and nonphysicians.

MATERIALS AND METHODS Internet-based surveys were administered to consumers of cosmetic procedures and physician members of the American Society for Dermatologic Surgery. Descriptive statistics and graphical methods were used to assess responses. Comparisons between groups were based on contingency chi-square analyses and Fisher exact tests.

RESULTS Two thousand one hundred sixteen commenced the patient survey with 401 having had a cosmetic procedure performed. Fifty adverse events were reported. A higher number of burns and discoloration occurred in the nonphysician–treated group and took place more often in a spa setting. Individuals seeing nonphysicians cited motivating factors such as level of licensure (type) of nonphysician, a referral from a friend, price, and the location of the practitioner. Improper technique by the nonphysician was cited most as a reason for the adverse event. Both groups agree that more regulation should be placed on who can perform cosmetic procedures. Recall bias associated with survey data.

CONCLUSION Patients treated by nonphysicians experienced more burns and discoloration compared with physicians, and they are encountering these nonphysicians outside a traditional medical office, which are important from a patient safety and regulatory standpoint. Motivating factors for patients seeking cosmetic procedures may also factor into the choice of provider.

KEY POINTS Both patients and physicians think more regulation should be in place on who can perform cosmetic procedures. More adverse events such as burns and discolorations occurred with patients seeing nonphysicians compared with those seeing physicians. In addition, for those seeing nonphysicians, a majority of these encounters took place in spa settings. Patient safety is of utmost concern when it comes to elective cosmetic medical procedures. More adverse events and encounters occurring outside traditional medical settings when nonphysicians performed these procedures call into question the required training and oversight needed for such procedures.

Supported by the American Society for Dermatologic Surgery—Future Leaders' Network as well as in part through the NIH/NCI Cancer Center Support Grant P30 CA008748. The authors have indicated no significant interest with commercial supporters with regard to this study.

There is an ongoing increase in the demand for medical, surgical, and cosmetic procedures.[1] According to the 2016 American Society for Dermatologic Surgery (ASDS) Survey on Dermatologic Procedures, members saw a significant increase in minimally invasive cosmetic treatments over the prior year. In 2016, there were over 3.3 million injectable neuromodulators and soft-tissue

*Department of Medicine, Dermatology Service, Memorial Sloan Kettering Cancer Center, New York, New York; †Department of Dermatology, Harvard Medical School, Massachusetts General Hospital, Boston, Massachusetts

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.dermatologicsurgery.org).

ISSN: 1076-0512 • Dermatol Surg 2019;45:588–597 • DOI: 10.1097/DSS.0000000000001829

filler procedures performed, and nearly 2.8 million were laser/light/energy-based procedures. In the past 5 years, there has been a 48% increase seen in soft-tissue filler procedures and 2.5 times increase in body contouring procedures performed.[2] Furthermore, the 2017 ASDS Consumer Survey on Cosmetic Dermatologic Procedures found that of the 7,322 people surveyed, nearly 7 in 10 are considering a cosmetic procedure. The top 4 of 11 factors influencing the selection of a practitioner included: price (49%), specialty in which the physician is board certified (41%), referral from a physician (37%), and level of licensure of the practitioner (32%).[3] This increased demand for cosmetic services has resulted in a substantial influx of nonphysicians offering cosmetic procedures and patients turning to nonphysicians for aesthetic medical treatments.[4] Nonphysicians are also starting to practice medicine independently in some states. Although originally intended for the shortage of primary care physicians, nonphysician providers (aestheticians, nurses, physician assistants, and nurse practitioners) are entering into specialty medical fields, even though formal medical training in these areas may be lacking. This is concerning from a patient safety standpoint.

Increasingly, nonphysicians are offering cosmetic procedures in a multitude of medical and nonmedical arenas. The boundaries between cosmetic surgery and cosmetology are obscured, with procedures being performed on otherwise healthy individuals by nonphysicians.[5] Although often promoted as a "quick fix," real risks and complications associated with these procedures may be marginalized.

Studies have also shown that dermatologists and nondermatologist physicians delegate cosmetic procedures to nonphysician providers to keep up with growth in demand.[4] This study seeks to determine the outcomes of cosmetic procedures performed by physicians and nonphysicians as well as the patient and physician perspectives of such. The authors describe the incidence and scope of adverse events as reported by both consumers and physicians. A better understanding of these outcomes will help guide physician oversight of these procedures and the training and regulations required of those who perform these procedures to ensure patient safety.

Methods

With IRB approval, Internet-based surveys (Survey Monkey: http://www.SurveyMonkey.com) were administered to consumers of cosmetic dermatology procedures and physician members of the ASDS. The consumer survey was web-based and opened by 2,116 consumers nationally via SurveyMonkey, which allows surveys to be distributed to a random prescreened population. The English language survey was distributed via email. The survey contained 24 multiple-choice questions related to provider type, setting where services were provided, and adverse events. Based on the question, participants were allowed to choose single or multiple responses, and responders were able to skip questions or stop the survey at any time (see **Supplemental Digital Content 1**, Appendix, http://links.lww.com/DSS/A131).

A separate physician survey was sent to members of the ASDS via email. This survey assessed members' opinions and experiences with cosmetic procedures performed by nonphysicians (see **Supplemental Digital Content 1**, Appendix, http://links.lww.com/DSS/A131).

After acquiring completed surveys, each was assessed individually by the investigators. Participants were allowed to stop the survey at any point and were allowed to skip questions. Statistical analysis and comparisons between groups were based on contingency chi-square analyses and Fisher exact tests.

Results

Consumer Survey (N = 2,116)

Demographics

Of the 2,116 surveys commenced by consumers, over half (55.9%) indicated that they either had a cosmetic procedure (19.1%, 401/2,098) or were considering having a cosmetic procedure (36.8%, 773/2,098)

TABLE 1. Demographics of Consumers

Descriptor	*Percent*
Gender	
Female	95.4
Male	4.6
Age	
Under 30	0.1
30–40	21.1
41–50	24.4
51–60	37.7
Over 60	16.6
Employment status	
Full time	69.0
Part time	10.9
Unemployed	1.9
Homemaker/retired/other	18.1

(Table 1). Of the patients who received cosmetic procedures, 145 went to a physician, 144 saw nonphysicians, and 97 have had procedures done by both physicians and nonphysicians. The remaining responders did not know the level of training of the individual who performed the procedure.

Scope of Procedures and Providers

The most common procedures consumers received were laser hair removal, injectable wrinkle-relaxing treatments, microdermabrasion, chemical peels, and injectable filler treatments (Table 2). Table 2 includes the breakdown of procedures reported to be done by nonphysicians as well as the percent of adverse events per procedure. Of the respondents who had a cosmetic procedure done by only a nonphysician, the top procedures performed included: laser hair removal, 49% (71); microdermabrasion, 35.9% (52); chemical peels, 23.4% (34); laser and light devices for facial problems, 13.8% (20); and injectable wrinkle-relaxing treatments, 13.1% (19). Most procedures performed by physicians were done by either a plastic surgeon (33.1%) or a dermatologist (32.3%). Other types of physicians included family practitioners, otolaryngologists, and vascular specialists (responders were able to choose more than one if applicable). Of the procedures performed by nonphysicians, the majority was performed by an aesthetician (43.5%) followed by a nurse (21.9%) (Table 3). Other nonphysician providers included nurse practitioners and laser technician.

Location of Cosmetic Procedures

The vast majority of consumer respondents who had their procedure performed by a physician identified the location as the physician's office (87.6%) ($p < .0001$). This was followed by a spa location (4.1%) or an aesthetician's office. By contrast, for patients who had their procedures performed by nonphysicians, this most often took place in a spa (36.8%, $p < .001$), followed by an aesthetician's office (25.7%, $p < .001$) and a physician's office (22.2%) (Table 4 and Figure 1).

Adverse Events

Fifty of the 404 respondents who had cosmetic procedures reported an adverse event (Table 5 and Figures 2 and 3). A total of 54% ($n = 27$) occurred in patients who saw physicians and 46% ($n = 23$) in patients who saw nonphysicians. The most common adverse events occurring in procedures performed by physicians were: "bruising" (40.7%, $n = 11$), "discoloration" (14.8%, $n = 4$), "scarring" (14.8%, $n = 4$), and "nerve damage" (14.8%, $n = 4$). In procedures performed by nonphysicians, the most common adverse events were "discoloration" (43.4%, $n = 10$), "burn" (34.7%, $n = 8$), and "bruising" (26.1%, $n = 6$)

TABLE 2. Consumer Survey: Scope of Cosmetic Procedures and Adverse Events

Procedure	*Total Number,* N *= 401, (%)*	*Nonphysician Procedures,* N *Answered = 144, (%)*	*Physician Procedures,* N *Answered = 149, (%)*	n *= Total No. of Participants Who Experienced a Complication*	*Percentage of Total Complications*
Laser hair removal	132 (33.0)	71 (49)	21 (14.1)	20	12.58
Injectable wrinkle-relaxing treatments	121 (30.3)	19 (13.1)	49 (32.9)	26	16.35
Microdermabrasion	120 (30.0)	52 (35.9)	120 (30.0)	21	13.21
Chemical peels	98 (24.5)	34 (23.4)	98 (24.5)	12	7.55
Laser and light treatment to reduce redness, improve skin tone, or improve scars	85 (21.3)	20 (13.8)	85 (21.3)	19	11.95
Injectable filler treatments	75 (18.8)	11 (7.6)	75 (18.8)	22	13.84
Varicose or spider vein treatments	72 (18.0)	8 (5.5)	72 (18.0)	15	9.43
Body sculpting (e.g., cryolipolysis, laser lipolysis, tumescent liposuction, and ultrasound fat reduction)	60 (15.0)	3 (2.1)	60 (15.0)	9	5.66
Ultrasound, laser, light, and radiofrequency treatments for skin tightening and wrinkle smoothing	50 (12.5)	10 (15.3)	50 (12.5)	11	6.92
Laser tattoo removal	6 (1.5)	2 (1.4)	6 (1.5)	3	1.89
Hair transplantation	3 (0.8)	1 (0.7)	3 (0.8)	1	0.63

Respondent can select multiple responses.

(Table 5). The difference in rates of discoloration and burns was significantly higher in procedures performed by nonphysicians compared with physicians ($p < .03$) (Figure 2). The occurrence of nerve damage after procedures performed was cited in 4 cases by the responders. All 4 physicians performing these were cited as nondermatologist physicians and the procedures performed included

TABLE 3. Consumer Survey: Provider Performing the Cosmetic Procedure (Responders Were Able to Choose More Than One)

Provider	*Number (%),* N *(%)*
Physician	
Plastic surgeon	82 (33.1)
Dermatologist	80 (32.3)
Facial plastic surgeon	21 (8.5)
Oculoplastic surgeon	2 (0.8)
I do not know	27 (10.9)
Other type of physician	36 (14.5)
Nonphysician	
Aesthetician	117 (43.5)
Nurse	59 (21.9)
Spa staff (other than aesthetician)	32 (11.9)
Physician assistant	17 (6.3)
I do not know	27 (10.0)
Other type of nonphysician	10 (3.7)

TABLE 4. Consumer Survey: Location of the Cosmetic Procedure by Provider (Responders Were Able to Choose More Than One)

Location	*Physician Provider*	*Nonphysician Provider*	*Fisher Exact* p*
Physician's office	127	32	<.0001*
Dental office	1	1	.749
Nurse's office	0	9	.002*
Aesthetician's office	6	37	<.001*
Physician assistance's office	1	2	.497
Spa	6	53	<.001*
I do not know	4	10	.082

*Statistically significant between the 2 groups compared.

neurotoxin (1), body sculpting (2), and varicose vein treatment (1). When adverse events are further sorted between dermatologists, plastic surgeons, other physicians, and nonphysicians, the rates of discolorations and burns are still higher for nonphysicians (Figure 3).

Consumer Viewpoint of Provider Qualifications

Consumers were asked which nonphysician providers were qualified to perform cosmetic procedures. A majority of respondents felt physician assistants (68.0%) and nurses (57.3%) were qualified to perform cosmetic medical procedures. Conversely, a majority felt that medical assistants (70.7%), aestheticians (57.9%), and spa staff other than aestheticians (90.8%) were not qualified (multiple responses were accepted).

If consumers selected "no," indicating that a particular group was not qualified to perform cosmetic medical procedures, 34.1% said it was because the individual was not a physician. Greater percentages of respondents said it was due to a lack of training (47.5%) or an inadequate level of training (75.4%). Responses under "other" included a "lack of accountability," "lack of experience handling difficult cases," and "no certifying or supervisory agency."

Consumer Motivation to Choose Provider

Consumers were asked what factors were important when choosing a provider for their cosmetic procedure (Figure 4). Of individuals who responded to this question and saw a physician ($n = 140$), the most important factors were board certification of physician (66.4%, $n = 93$, $p < .0001$), referral from a physician (59.3%, $n = 83$), number of procedures performed (37.1%, $n = 52$), and level of licensure of physician (36.4%, $n = 51$). For those who responded to this question and saw nonphysicians ($n = 137$), the most important factors were level of

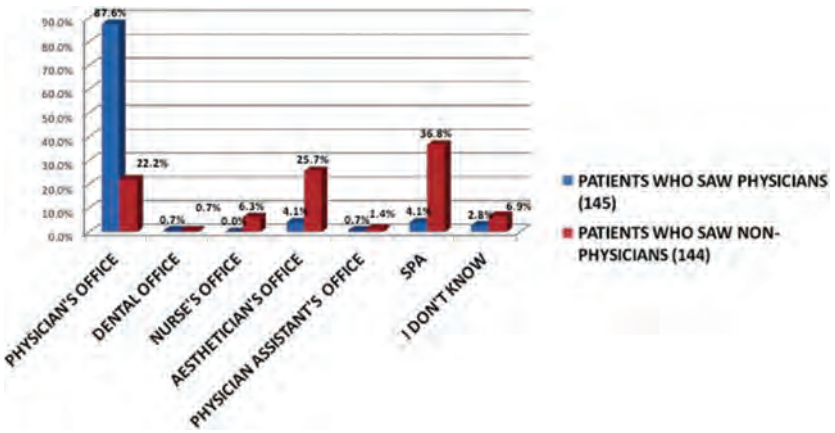


Figure 1. Graph of location of the cosmetic procedure by a provider (responders were able to choose more than one).

TABLE 5. Consumer Survey: Statistically Significant Adverse Events by a Provider (Responders Were Able to Choose More Than One)

Adverse Event	*Physician Provider (*N *= 27 Responded),* N *(%)*	*Nonphysician Provider (*N *= 23 Responded),* N *(%)*	*Fisher Exact* p
Discoloration	4 (14.8)	10 (43.5)	.031*
Burn	2 (7.4)	8 (34.8)	.03*

*Statistically significant between groups.

licensure (59.1%, $n = 81$, $p < .0001$), referral from a physician (48.2%, $n = 66$), and referral from a friend (41.6%, $n = 57$, $p < .05$). Price ($p = .053$) and the location of the practitioner ($p < .005$) were also important for those seeing nonphysicians. Consumers who responded with the "other" option cited patient reviews, web sites, and the complexity of the procedure as motivating factors for choosing a practitioner.

*Physician Survey (*N *= 118 Responses)*

Dermatologic Surgeon Treatment of Cosmetic Complications

This survey assessed the types of complications that physicians have encountered with cosmetic procedures performed by nonphysicians. Of the 118 ASDS members who responded to the survey, 65 (55%) stated that they treated a complication from a cosmetic procedure performed by a nonphysician. Most respondents (43.1%) reported treating 1 to 3 complications, whereas 24.6% treated 4 to 6 complications, and 7.7% treated complications 7 to 9 times.

Nearly a quarter of respondents (24.6%) reported treating 10 or more cases of complications resulting from cosmetic procedures performed by nonphysicians (Figure 5).

American Society for Dermatologic Surgery members were then asked to select which types of complications they observed following cosmetic procedures performed by nonphysicians. The most common adverse event was a burn (67.2%) followed by misplacement of a filler product (53.1%). Other common complications included facial drooping (34.4%), tissue deformity (29.7%), and bruising (28.1%). "Other" responses included hypopigmentation or hyperpigmentation, leg ulcers, and scarring (Figure 5).

Physicians were then asked to evaluate the most likely contributing factors for the adverse events that were encountered. The most common response was improper technique (43.8%) followed by improper settings (12.5%). Less than 10% of complications were considered an expected adverse event (Figure 6).

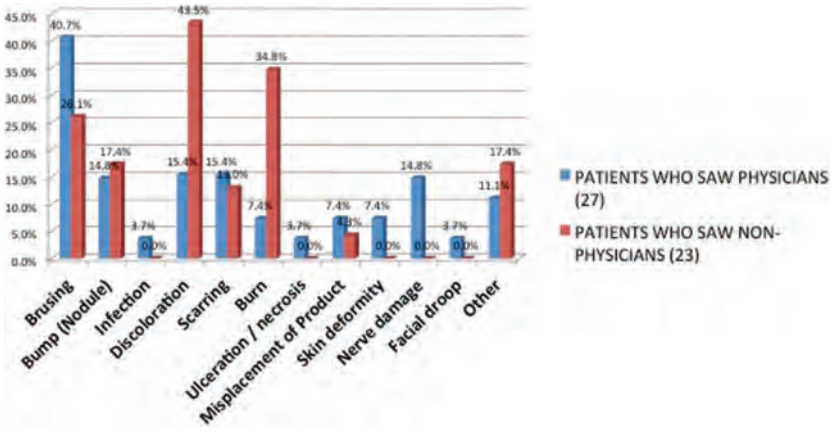


Figure 2. Graph of consumer survey: adverse events by a provider (responders were able to choose more than one).

ATTACHMENT D

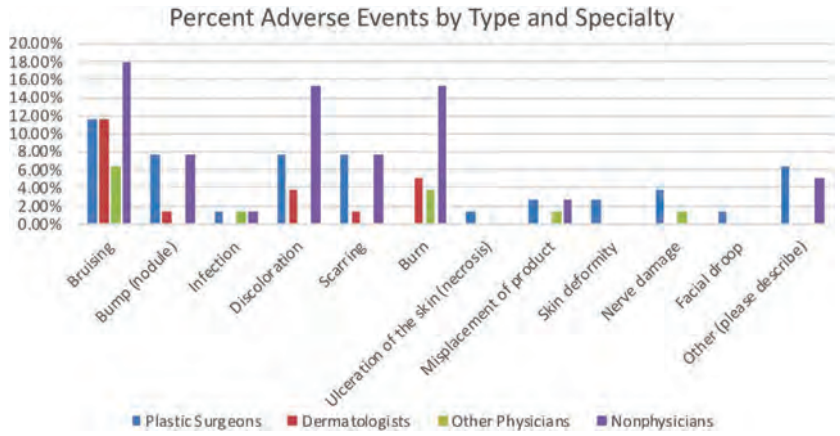


Figure 3. Graph of consumer survey: percent of adverse events stratified by dermatologists, plastic surgeons, and nonphysicians (responders were able to choose more than one).

Regulation of Cosmetic Procedures

Both physician and consumers were polled as to whether there should be stricter regulations on who can perform cosmetic procedures. The majority of ASDS members (86.3%) said there should be stricter regulation. Of the consumers surveyed, a majority (85.8%) also said there should be stricter regulations. There was no difference between the physician group and consumers group (p = .88).

Discussion

The demand for cosmetic medical procedures continues to rise and patients are seeking treatment in a variety of settings by both physicians and nonphysicians. This undersupply of board-certified dermatologists has had a significant impact on patient access to care and has resulted in long wait times with patients seeking alternative providers for their care.[1,6] The performance of cosmetic procedures warrants close inspection and a survey of the current landscape of procedures being performed, as it is important to understand who is performing these procedures, the adverse event profiles, and outcomes. A major finding of this study was that the majority of cosmetic procedures being performed by nonphysicians took place outside of a traditional medical office setting. Procedures occurring in other settings may raise concerns regarding oversight, standards, and regulations that are in place to protect patients and ensure safety. In addition, burns and discolorations were cited as the most common adverse events encountered by patients treated by nonphysicians.

Adverse Events

Overall, numbers of adverse events were quite low in this study, with only 50 adverse events reported by

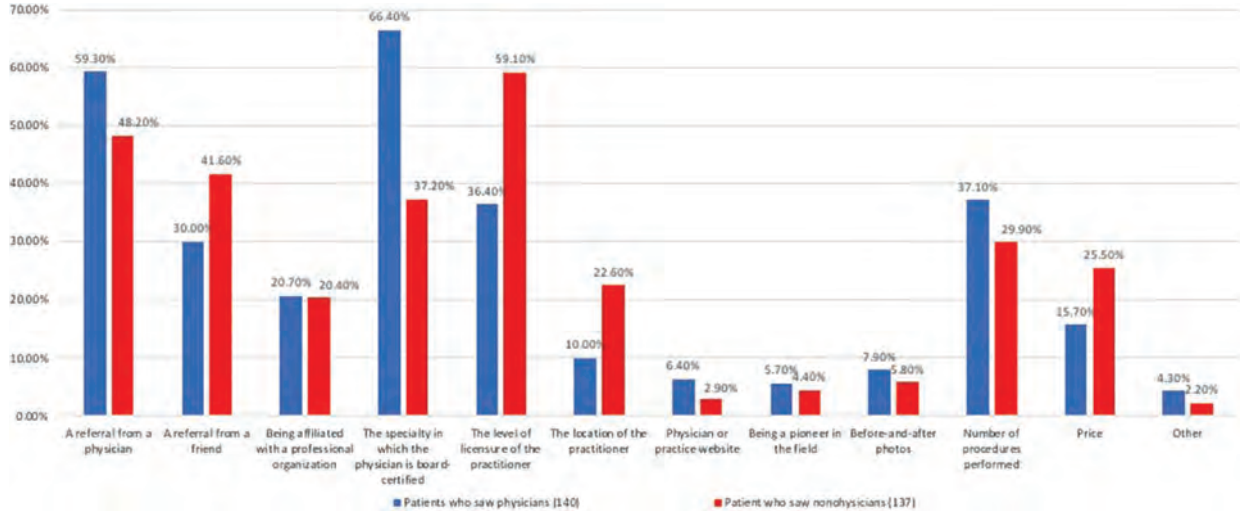


Figure 4. Consumer motivating factors for choosing a physician versus nonphysician.

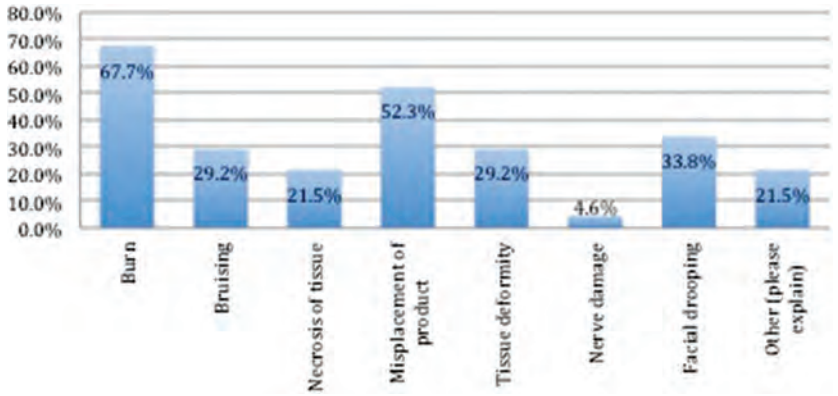


Figure 5. Physician survey: types of complications following procedures performed by a nonphysician.

consumers, the nature of which is in line with reports regarding the safety of dermatologic cosmetic procedures.[7] Although this study looks at both physicians and nonphysicians, this number may underestimate the actual prevalence, as reporting of adverse events is not mandatory, especially for procedures that take place outside of a physician's office. Of the specific adverse events, there was a statistically significant greater difference in the rates of discoloration and burns in the nonphysician group compared with the physician group. This echoes previous published reports by Jalian and colleagues[8] of a higher rate of litigation for laser burns when performed by nonphysicians. The burns and discoloration experienced by patients after procedures performed by nonphysicians may result from inadequate training in how the skin responds to cosmetic procedures (such as lasers) or from insufficient training in selecting the ideal patient and appropriate laser parameters. The majority of adverse events reported by consumers who saw physicians was bruising, and bruising can be an expected part of certain procedures. Of note, the prevalence of nerve damage was reported by consumers, which approached significance in the physician-treated group. None of the nerve damage was cited as permanent, and the procedures performed included neurotoxin (1), body sculpting (2), and varicose vein treatment (1). It was not gauged as to what type of, sensory or motor, impairment occurred in these 4 cases.

Consumer Viewpoint of Qualified Providers

Consumer motivation is a major factor in aesthetic medicine. A further understanding of the motivating factors that drive patients to certain practitioners is important for comprehending the role of nonphysicians. Regarding provider qualification, consumers favored nurses and physician assistants to perform cosmetic medical procedures over other nonphysicians. However, this is interesting because a majority of patients in this survey treated

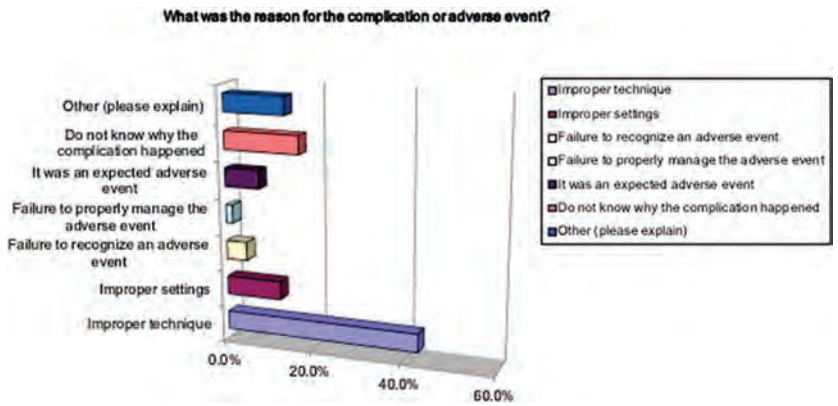


Figure 6. Physician survey: suspected reason for the adverse event when performed by a nonphysician.

by nonphysicians were treated by an aesthetician. This suggests that there are competing factors, such as location, affordability, and persuasive marketing strategies, in place that effectively entice patients into having cosmetic procedures in nonmedical settings by those that they perceive as less qualified. This could also echo previous American Medical Association surveys showing that patients may not understand the different levels of licensure or types of nonphysician providers.[9]

American Society for Dermatologic Surgery Members' Responses

Almost a quarter of ASDS members reported treating 10 or more complications from procedures performed by nonphysicians. This number is higher than consumer-reported complications and could underscore the notion that most complications go unreported by patients or providers. From the complications that ASDS members reported treating, a laser burn was the most common adverse event, which reinforces recent literature and the authors' own results from this study. Interestingly, misplacement of a filler product was the second most common event, and "improper technique" was cited as the most common reason. Anatomy knowledge, injection technique, and selecting appropriate patient cases to perform are all factors that could contribute to this. Other physician surveys have shown that although the majority of physicians feel nurses are capable of administering vaccines, they are not as capable as physicians at administering injectable cosmetic procedures.[10,11] This could be because of the nature of the procedures, a physician's in-depth knowledge and hands on training in anatomy, and the complexity involved. In this study, over 85% of dermatologic surgeons and consumers alike said there should be stricter regulation over who can perform cosmetic procedures. Clarification on training requirements and scope of practice guidelines might help ensure standards are upheld and patient safety is preserved.

Limitations

This study has limitations due to the nature of survey-based research and inherent response bias. This was an email-based survey that may also not fully capture the complete demographic of consumers, and patients were not asked how many times they had a procedure performed. Also, as previous American Medical Association surveys have shown, patients may not know the exact degree or title of the treating practitioner, which may have influenced their ability to accurately respond to questions. Physician members of the ASDS were not asked specifically about adverse events that resulted from cosmetic procedures performed by other physicians. Other studies have shown that cosmetic procedures are performed by various specialties outside of dermatology, including: general surgery, otolaryngology ophthalmology, facial plastic surgery, family medicine, pediatrics, and internal medicine.[12] Future studies are warranted to better characterize adverse events following physician-performed cosmetic procedures, as this may call into question scope of practice of various providers.

Conclusion

Adverse events reported by consumers following cosmetic procedures are infrequent, but still occur. The most common types of adverse events reported with cosmetic procedures performed by nonphysicians are burns and discoloration. This contrasts adverse events from procedures performed by physicians in this study, which consisted mainly of bruising, which does not imply a complication per se. A majority of patients seeing nonphysicians are encountering them outside the traditional medical office, including spas. This could reflect the growing number of "medispas" that are being operated by nonphysicians and could represent a potential concern for safety and regulation. Attention should be given to this alarming trend, as these untraditional settings may not be held to medical practice standards and have inadequate oversight from qualified physicians. Moving forward, the authors need improved data collection on adverse events and outcomes, which may help guide regulations and oversight necessary for providing quality care and ensuring patient safety.

Acknowledgments The authors are grateful to the American Society for Dermatologic Surgery—Future Leaders' Network and staff for contributing to this project, including Tamika Walton, Jolene Kremer,

Debra Kennedy, and Katherine Duerdoth. The authors thank Stephen Dusza, DrPH, for his work on the statistical analysis of this project.

References

1. Kimball AB, Resneck JS Jr. The US dermatology workforce: a specialty remains in shortage. J Am Acad Dermatol 2008;59:741–5.
2. American Society for Dermatologic Surgery. *2016 ASDS Survey on Dermatologic Procedures*. 2017. Available from: https://www.asds.net/2016-procedures-survey.aspx. Accessed November 1, 2017.
3. American Society for Dermatologic Surgery. *2017 ASDS Consumer Survey on Cosmetic Dermatologic Procedures*. 2017. Available from: https://www.asds.net/consumer-survey/. Accessed October 1, 2017.
4. Austin MB, Srivastava D, Bernstein IH, Dover JS. A survey comparing delegation of cosmetic procedures between dermatologists and nondermatologists. Dermatol Surg 2015;41:827–32.
5. Brody HJ, Geronemus RG, Farris PK. Beauty versus medicine: the nonphysician practice of dermatologic surgery. Dermatol Surg 2003;29:319–24.
6. Suneja T, Smith ED, Chen GJ, Zipperstein KJ, et al. Waiting times to see a dermatologist are perceived as too long by dermatologists: implications for the dermatology workforce. Arch Dermatol 2001;137:1303–7.
7. Alam M, Kakar R, Nodzenski M, Ibrahim O, et al. Multicenter prospective cohort study of the incidence of adverse events associated with cosmetic dermatologic procedures: lasers, energy devices, and injectable neurotoxins and fillers. JAMA Dermatol 2015;151:271–7.
8. Jalian HR, Jalian CA, Avram MM. Increased risk of litigation associated with laser surgery by nonphysician operators. JAMA Dermatol 2014;150:407–11.
9. American Medical Association Advocacy Resource Center. *Truth in Advertising*: Campaign Booklet; 2015. Available from: http://ama-assn.org/go/tia. Accessed April 5, 2018.
10. Small K, Kelly KM, Spinelli HM. Are nurse injectors the new norm? Aesthet Plast Surg 2014;38:946–55.
11. Resneck JS Jr, Kimball AB. Who else is providing care in dermatology practices? Trends in the use of nonphysician clinicians. J Am Acad Dermatol 2008;58:211–6.
12. Housman TS, Hancox JG, Mir MR, Camacho F, et al, What specialties perform the most common outpatient cosmetic procedures in the United States? Dermatol Surg 2008;34:1–7; discussion 8.

Address correspondence and reprint requests to: Anthony M. Rossi, MD, Department of Medicine, Dermatology Service, Memorial Sloan Kettering Cancer Center, 16 East 60th Street, 4th Floor, New York, NY 10022, or e-mail: RossiA@mskcc.org

ATTACHMENT D

Valley women claim botched lip injections caused severe infection

By Jennifer Martinez | **Published** August 18 | **Updated** August 19 | Crime and Public Safety | FOX 10 Phoenix

PHOENIX - They're all the rage for some women - pouty lips. To get the look, they're paying to have lip injections. Which works out for most, but several Valley women are dealing with a nightmare after their lip injections were botched. We want to warn you - the photos you're about to see are pretty graphic.

We spoke to seven girls who say they went to the house willingly to get lip injections. They tell us they had been recommended by other people who have gone previously and had good results. What these girls have in common is August third. They didn't know each other beforehand but met after their lips were infected.

ATTACHMENT D

Again, we want to warn that these images are graphic. Swelling, cold sores, pus, and much more.

On August third, these girls went to a home in Maricopa to get lip injections. Instead, they left with their lips infected.

"Right after I left getting my lips done - an hour later, my lips got huge, like, giant," said Alexandra Garaventa, who claims lip injections caused infection.

"The pain after was so bad, I couldn't even feel my lips," said Ashleigh Villaverde, who also claims lip injections caused infection. "We couldn't even sit there and go to bed, our lips were throbbing."

The girls say the woman who performed the procedure came highly recommended and at a low cost.

"It was cheaper, that's not the smartest thing but since I had seen so many people and my friend had been going for a year," Garaventa said. "She was telling people that she was certified to do lip injections and since I [had] seen other people's [lips], I had decided why not go."

Villaverde says this wasn't her first time going to the woman to get her lips done. In fact, she had gone several times before. But this time, it felt different.

"As soon as I went this time, I knew something was wrong because each time I injected, it hurt so bad," Villaverde said. "That has never happened before. They have swelled up, but never to the point that I couldn't even touch them."

ATTACHMENT D

The girls rushed to the emergency room hours after the injections. Some were admitted to the hospital, with doctors not knowing what was put into their lips.

"When I came in, they already knew what was going on," said Nayhely McLaughlin, who claims lip injections caused infection. "They asked if I went to Maricopa - we just had, like, eight girls here yesterday."

The girls say the woman would charge $80 a milliliter. The average cost is $600. We headed to the home where this happened and there was no answer at the door.

"We don't know if it's going to have good or bad results," McLaughlin said. "If we're going to have scars, we don't know if it's going to leave us ugly. We don't know if it's going to leave us ugly or start to rot."

The girls also tell us the woman would only do these procedures on Saturdays, going on to say she allegedly had more than 20 people waiting to get this procedure done.

The Maricopa Police Department has been notified. We have reached out to them and we're waiting to hear back. As for the girls., they say they've learned their lesson and will be going to a professional if they want injections.

ATTACHMENT D

ATTACHMENT D

Op-Ed: Practicing Medicine vs Practicing Advanced Nursing

— "Most of the time I was OK. The problem was that I couldn't recognize when things were not OK"

by Rebekah Bernard, MD
November 29, 2020
Last Updated November 30, 2020

The following is an excerpt from a new book, Patients at Risk: The Rise of the Nurse Practitioner and Physician Assistant in Healthcare*, by Rebekah Bernard, MD, and Niran Al-Agba, MD.*

What is the difference between the practice of medicine and the practice of advanced nursing?

Advocates say that nurse practitioners are capable of autonomously diagnosing and treating acute and chronic medical conditions. While this sounds like the practice of medicine, nurse practitioners insist that they do not practice medicine, but rather, they practice "advanced nursing." What is the difference, and why is the distinction important? Orla Weinhold, MD, a physician who was a family nurse practitioner for eight years before attending medical school characterizes the differences. "Nurse practitioners are taught pattern-based thinking, and physicians are taught more critical thinking." Another physician who was a nurse practitioner first, Dara Grieger, MD, agrees. "As a nurse practitioner, I was taught to recognize the patterns but not the 'why' behind them." What Weinhold and Grieger describe as the difference in the way that nurses and doctors think is the difference between forward reasoning and backward reasoning.

Nursing education tends to emphasize a reverse reasoning methodology because it uses a framework built upon symptom identification from patterns rather than a diagnostically driven focus. There is nothing inferior about this method. It is a necessary technique when caring for patients at the bedside.

"Nursing is not medicine and medicine is not nursing. We care about different things," says Nixi Chesnavich, DO, a physician who worked as a nurse for ten years before attending medical school. "Nursing theory is what the patient would do for themselves if they

ATTACHMENT D

understood or had the information or could physically perform themselves." To provide this care, nurses learn to follow a multi-step framework called the "Nursing Process."

In following this process, nurses become intimately acquainted with their patients, particularly when they are working at a patient's bedside. Joann D'Aprile, DO, worked as a nurse and taught nursing school before becoming a physician. "Nurses identify the biopsychosocial needs of patients, provide symptom relief and comfort, and assist patients in regaining optimal function." She compares the care that nurses give to that of a mother caring for an ill child. "Add in a fundamental understanding of the human body and condition, and what types of nursing interventions will help that person regain your health; that is nursing." D'Aprile also adds that the role of the nurse is to advocate for the patient. "If there is an error in an order, a nurse would bring the issue to the physician's attention." Truly, there is nothing like a nurse.

Medicine follows a different model. Cheryl Ferguson, MD, is a physician who worked as a nurse and even attended a semester of nurse practitioner school before she decided to pursue medical school. Ferguson notes that nursing is "knowing how to take care of patients' needs, whether they are physical, social, psychological. Medicine is much more scientific; diagnosing the disease, not just the symptoms, weighing risks and benefits of treatment, understanding lab results and what they really mean. Nursing is not medicine. Medicine is not nursing. They overlap but should be separate entities to be best for patient care."

ATTACHMENT D

Rather than focusing on the moment-to-moment needs of the patient, physicians are trained to search for one unifying diagnosis for their symptoms and focus on the most effective way to manage their disease process. This does not mean that physicians do not deeply care about the patient's biopsychosocial needs. Henry Travers, MD, notes that just like nurses, physicians are also interested in becoming intimately acquainted with the patient and providing symptom relief and comfort. Travers says, "the point is that the total care of the patient is critically dependent on the correct diagnosis while being mindful of the difference between disease and illness."

The difference in models may be one of the reasons that patients value nurses so highly. Indeed, the work done by nurses should be highly valued by everyone in healthcare. There is nothing that can replace the one-on-one personal attention and care that a good nurse provides. But patients also need a diagnostician -- someone who can determine why they have a medical symptom -- and ideally, help them to recover fully. This is where physician-training focuses. The training provided for a registered nurse as described in the nursing process does not provide the tools to independently diagnose and treat patients.

Can a nurse practitioner gain the necessary knowledge to take on this role in an additional two years of training? Physicians who were previously nurse practitioners say no. The biggest reason: nurse practitioner school did not adequately prepare them to be able to develop an adequate differential diagnosis, the essential list necessary to accurately diagnose disease.

Nurse practitioners do not have the time or in-depth training during a two-year program to learn how to develop a comprehensive differential diagnosis. Orla Weinhold, MD, notes, "When I was a nurse practitioner, I never knew how to form a differential diagnosis. This was one of the most challenging parts of my clinical rotations in medical school. I didn't know how much I didn't know."

Ronald Epstein, MD, writes in *Attending: Medicine, Mindfulness, and Humanity* (2017) that even a non-medical person can learn how to recognize the signs and symptoms of various medical ailments and be correct most of the time. The need for physician training occurs during those rare times when a medical situation is unusual or more complicated -- and potentially life-threatening. Epstein argues that this is the very reason for the long and arduous journey of medical training. Without additional training on how to perform a

ATTACHMENT D

differential diagnosis and the fund of knowledge required to expand the potential diagnoses to include the most serious causes of a patient's symptoms, non-physician practitioners may put patients at risk.

Fortunately, most of the time, patients do not present with a critical illness or life-threatening problems. The problem arises with the occasional patient who truly needs an expert diagnostician. As Dara Grieger, MD, notes, "As a nurse practitioner, most of the time I was OK. The problem was that I couldn't recognize when things were not OK."

Rebekah Bernard, MD, is a family physician in Fort Myers, Florida, and president of Physicians for Patient Protection.

ATTACHMENT D

Original Article

Practice-Based Learning in Aesthetic Medicine: Assessing Scientific Literacy Among Cosmetic Practitioners

Fadia Fakhre, MS-II,* and Danny J. Soares, MD*†

BACKGROUND The field of aesthetic medicine has expanded substantially in the past decade, with significant practitioner diversification and departure from core-specialty supervision. The increased autonomy of nonphysician practitioners in a rapidly evolving field has raised accentuated the importance of scientific literacy and practice-based learning standards in the delivery of aesthetic medical care.

OBJECTIVE To assess the degree of scientific literacy among aesthetic medicine practitioners of different educational and training backgrounds in the United States and abroad.

MATERIALS AND METHODS A cross-sectional survey of 52 national and international aesthetic medicine practitioners employing a validated, 28-item, scientific literacy tool.

RESULTS The average score for all participants was 76% (SD = 18%, range = 43%–100%). Physician practitioners scored higher in all competencies compared non-physicians (86% vs 68%, $p < 0.001$), with a greater discrepancy among US practitioners (95% vs 71%, $p < 0.001$). Competencies relating to identification of bias/confounding variables, graphical data representation, and statistical inference/correlation showed the lowest proficiency. Practitioners with a doctorate or equivalent degree were significantly more likely to report frequent engagement with medical literature than non-physicians ($p = 0.02$).

CONCLUSION There exists a significant disparity in scientific literacy between physician and nonphysician aesthetic medicine practitioners. This gap underscores the need for enhanced educational programs and continuous professional development to ensure safe and effective patient care in the evolving field of aesthetic medicine.

The field of aesthetic medicine has witnessed substantial growth in the past decade, owing to a surge in the popularity of noninvasive cosmetic treatments.[1] This rise in demand has led to a notable shift in service provision, with nonphysician practitioners (NPPs, e.g., nurse practitioners, physician assistants, registered nurses, etc.), now representing a majority of treatment providers in the US medical spa setting.[2] The increased autonomy and gradual loss of core-specialty direct supervision (i.e. dermatology and plastic surgery) in aesthetic medicine has positioned NPPs at the forefront of aesthetic treatment delivery in many US states, often with limited specialty training, leading to an increased risk of suboptimal outcomes, adverse events, and litigation.[3–5] The sharp rise in the incidence of cosmetic treatment complications, including a significant rise in reported cases of filler-induced ischemic skin injury/blindness and adverse events related to laser treatments, has recently added further scrutiny into NPP training and clinical proficiency.[6–10]

Accordingly, regulatory bodies, including the US Food and Drug Administration, have delineated an increased need for standardized practitioner education and supervision in aesthetic medicine.[11,12] Among them, practice-based learning components, such as the ability to critically evaluate and synthesize evidence from the published literature, are regarded as vital aspects of graduate medical training.[13,14] Given the differences in foundational competencies and medical training of physicians and nonphysicians, it is plausible that disparities in scientific literacy exist, potentially influencing the quality of evidence-based medical practice.[15] The aim of this study was to assess the scientific literacy of aesthetic medicine practitioners from various medical and academic backgrounds, both within the United States and internationally.

Methods

A cross-sectional survey study was conducted in accordance with the Good Practice in the Conduct and Reporting of Survey Research endorsed by the Network for Enhancing the Quality of Transparency of Health Research.[16,17] Study participants were anonymously recruited from Facebook groups dedicated to aesthetic medicine containing national and foreign practitioners. The recruitment strategy targeted practitioners through social media outreach on Instagram and Facebook, with participation being voluntary and

From the University of Central Florida, College of Medicine, Orlando, FL; † American Foundation for Aesthetic Medicine (AFFAM), Fruitland Park, FL*

The author has indicated no significant interest with commercial supporters.

Address correspondence and reprint requests to: Danny J. Soares, MD, The Village Institute of Plastic Surgery, 607 Co Road 466A, Fruitland Park, FL 34731, or e-mail: drsoares@plasticsurgeryvip.com

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the full text and PDF versions of this article on the journal's Web site (www.dermatologicsurgery.org).

Dermatol Surg 2024;50:441–445
http://dx.doi.org/10.1097/DSS.0000000000004098

nonincentivized. Practitioners were included in the study if they were actively employed as treatment providers in the practice of aesthetic medicine, inclusive of cosmetic dermatology and plastic surgery. The survey offered a validated assessment tool—the Test of Scientific Literacy Skills (TOSLS, See **Supplemental Digital Content**, Appendix S1, http://links.lww.com/DSS/B374, for a copy of the survey)—allowing participants to evaluate their own proficiency in different domains of scientific literacy.[18]

Data Collection and Analysis

The survey was administered online, hosted on the Flexiquiz platform (NextSpark Pty Ltd, Victoria, Australia). Participants were allotted 1 hour to complete the survey, designed for a completion time of <35 minutes. To prevent duplicate submissions, the built-in features of the platform enabled IP address monitoring and disallowed resubmission once a survey had been completed and submitted. Relevant demographic information was collected, including country of practice, medical license type, highest attained academic degree, and aesthetic practice experience. Additionally, information pertaining to the frequency of reading published medical literature and perceptions on the importance of scientific literacy was also obtained.

The scientific literacy assessment comprised a 28-item test, measuring proficiency in 9 distinct skills (See **Supplemental Digital Content**, Table S1, http://links.lww.com/DSS/B373, which provides a description of each scientific literacy skill). These skills included evaluating experimental hypotheses, identifying bias and confounding factors, interpreting graphical data, solving algebraic equations, and drawing inferences from statistical analyses. Survey data were exported and assorted through Microsoft Excel software Version 15.51 (Microsoft Corp., Redmond, WA). Numerical data, including raw test scores, were assessed for normalcy using Kolmogorov–Smirnov and Shapiro–Wilk tests. Statistical analysis of group means was performed using an unpaired, 2-tailed Student *t*-test for 2 groups and a 1-way analysis of variance for comparison of means of more than 2 groups. For categorical data, a chi-square test was used for analysis of multiple proportions and a Fisher exact test for 2 × 2 contingency tables. Statistical testing was carried out via the Statistical Package for Social Sciences Software (SPSS, IBM Corp., Armonk, NY) with the significance threshold set at $p < .05$.

Results

Out of 86 individuals who accessed the digital link, a total of 52 participants completed the survey and the Test of Scientific Literacy Skills (TOSLS). Of these, 27 providers (52%) were based in the United States, whereas 25 (48%) practiced abroad, predominantly in Europe (88%). Table 1 displays descriptive data pertaining to participant's background. Nonphysician practitioners comprised 60% of respondents, with nurse practitioners, nurses, and physician assistants representing 39%, 32%, and 7% of NPPs, respectively. Expectedly, physician participants were significantly more likely to possess a doctorate degree or equivalent than NPPs (100% vs 16%, $p < .001$). Both physician practitioners and NPPs reported similar time dedicated to aesthetic medicine and comparable medical experience. Additionally, both physicians and NPPs were equally likely to regard scientific literacy as being very important to aesthetic practice, though practitioners with a doctorate were more likely to more frequently engage with the medical literature than those without (81% vs 46% reading the literature daily/weekly, Chi-Square $p = 0.02$).

The mean TOSLS score for all respondents was 21.2 of 28, representing a 76% grade (SD = 18%, median = 71%, range = 43%–100%). Figure 1 illustrates the comparative performance between physicians and nonphysicians. Physicians consistently outperformed NPPs in total scores and across nearly all scientific literacy competencies (86% vs 68%, $p < .001$), with a more pronounced difference among US-based practitioners (95% vs 71%, $p < .001$). When considering the highest academic degree attained, individuals with a doctorate ($n = 26$) scored significantly higher on the TOSLS than those without ($n = 26$; 85% vs 67%, $p < .001$). No significant difference in average TOSLS score existed among NPPs from different medical licensing backgrounds, including nurse practitioners (score = 69%), registered nurses (64%), and physician associates and others (71%), with $p = .62$. Figure 2 presents the score distribution of physicians and nonphysicians across each domain of scientific literacy. The most notable disparities in proficiency were observed in identifying bias/confounding variables, interpreting graphical data, solving algebraic equations, and skills relating to statistical inference/correlation.

Discussion

The modern standard of graduate education for medical practitioners has evolved beyond medical knowledge and patient care to include components that afford increased dynamism and adaptability.[19] Among these, competencies pertaining to practice-based learning and systems-based practice reflect the ever-evolving field of medicine and its structure.[20] For the former, the ability to "appraise and assimilate new scientific evidence into clinical practice" is of vital importance in the formative development of practitioners who can recognize and maintain evidence-based standards.[21] Hence, scientific literacy is critical to the practice of medicine, regardless of specialty, because it underpins the ability of practitioners to provide safe, effective, and evidence-based care.

The rapid evolution of aesthetic procedures and the introduction of new technologies and products demand that practitioners remain current with the latest research to avoid adverse outcomes. This aspect has become increasingly pertinent as of recent, given the rapid rise in the incidence of devastating complications with injectable treatments.[22] By staying informed through review of the latest literature, practitioners can adopt updated best practices, understand early signs of complications, and apply effective mitigation strategies. Moreover, the ability to critically appraise scientific information is crucial in

distinguishing between high-quality evidence, pseudoscience, and marketing-driven claims, which are particularly relevant, given the commercial pressures and influences affecting the field.[23]

With the surge in demand for aesthetic procedures, the administration of cosmetic treatments has shifted toward the realm of nonphysician practice, often with non-core specialty supervision, despite significant risks. A recent comprehensive survey of medical spas in the state of Florida demonstrated that NPPs comprise up to 86% of treatment providers, with an increasing number of facilities relying on autonomous practitioners.[2] Given the innate differences between competency-based physician training and the evolving nature of nonphysician education, some potential gaps in NPP instruction have been recognized, including the lack of consistent practice-based learning components.[15] The lack of sufficient training in the evaluation of scientific evidence may influence practitioner selection of therapeutic options, potentially affecting patient care.[24]

In this study, physicians were more likely to engage with the medical literature more frequently than NPPs, suggesting that practice-based learning components of resident training are effective in instilling awareness of the need for continuous, self-driven learning. In addition, the significant disparity in scientific literacy between the 2 groups, which aligned most significantly with a medical doctorate, validates the current Accreditation Council (ACGME) for Graduate Medical Education competency-based approach to resident training, with an average US physician TOSLS score of 95%. Among the domains reflecting the most significant disparity in proficiency, the identification of bias/confounding variables, interpretation of graphical data, and ability to draw inferences from statistical analysis were the most salient. These skills are essential to the critical evaluation of medical literature, representing areas where further emphasis in NPP training may be warranted and for which core-specialty supervision is likely to remain beneficial. For the present, it is critical to recognize the value of core-specialty physician oversight in ensuring adherence to updated practices, evidence-based therapies, and established safety standards in aesthetic medicine.

Despite being the first study evaluating the scientific literacy among aesthetic practitioners, several study limitations should be acknowledged. The limited sample size, although sufficient for initial analysis, may not capture the full diversity of aesthetic medicine

TABLE 1. Demographic and Medical Training/Academic Characteristics of Physician and Nonphysician Participants

Characteristic	Physicians	Nonphysicians	*p*
Sample size	*n* = 21	*n* = 31	
Practice location			
United States	13 (62%)	14 (45%)	.27
Europe	6 (29%)	14 (45%)	
South America	2 (10%)	1 (3%)	
Asia	0	2 (7%)	
Medical license			
Medical doctor (MD, DO)	21 (100%)		
Nurse practitioner		12 (39%)	
Registered nurse		10 (32%)	
Physician assistant		2 (6.5%)	
Dentist		4 (13%)	
Pharmacist		2 (6.5%)	
Technician		1 (3%)	
Percentage of clinical time dedicated to aesthetic medicine practice	74%	73%	.96
Years in practice			
<5 yrs	8 (38%)	17 (55%)	.60
5–10 yrs	4 (19%)	6 (19%)	
10–20 yrs	7 (33%)	6 (19%)	
>20 yrs	2 (10%)	2 (7%)	
Highest attained academic degree			
Doctorate or equivalent	21 (100%)	5 (16%)	<.001
Master's		20 (65%)	
Bachelor's		6 (19%)	

DO, Doctor of Osteopathic Medicine.

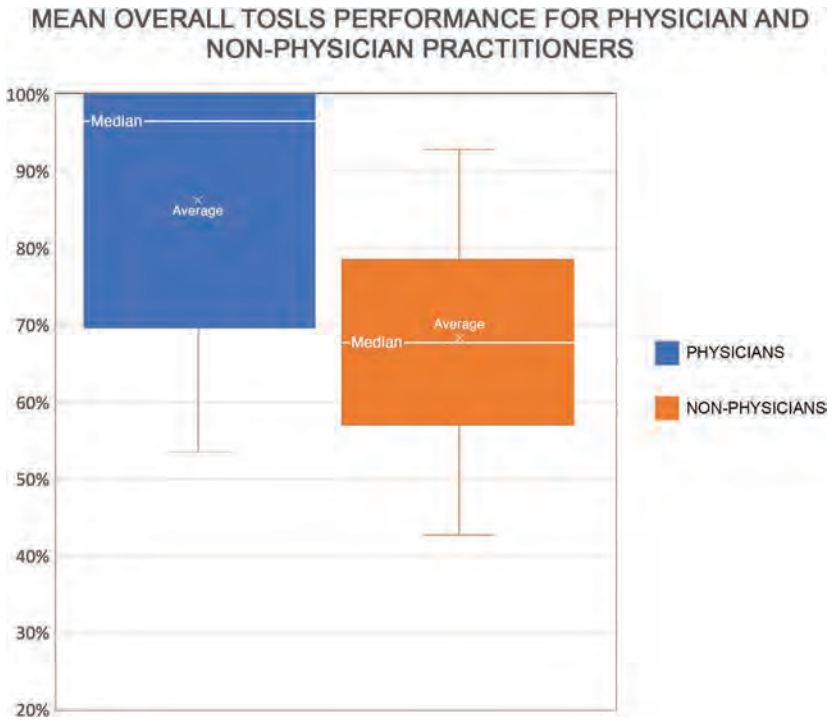


Figure 1. Boxplot of overall scores for physicians and nonphysicians on the test of scientific literacy skills.

practitioners, limiting the generalizability of the results. In addition, the recruitment method, which leveraged social media, may introduce selection bias by excluding those practitioners less engaged with online communities. Furthermore, the reliance on self-reported data could lead to inaccuracies relating to practitioner credentials or performance, and the online testing format precluded verification of testing conditions and foreign participants' credentials or English comprehension. These factors necessitate a cautious interpretation of the findings and point toward the need for methodological enhancements in future research on this topic.

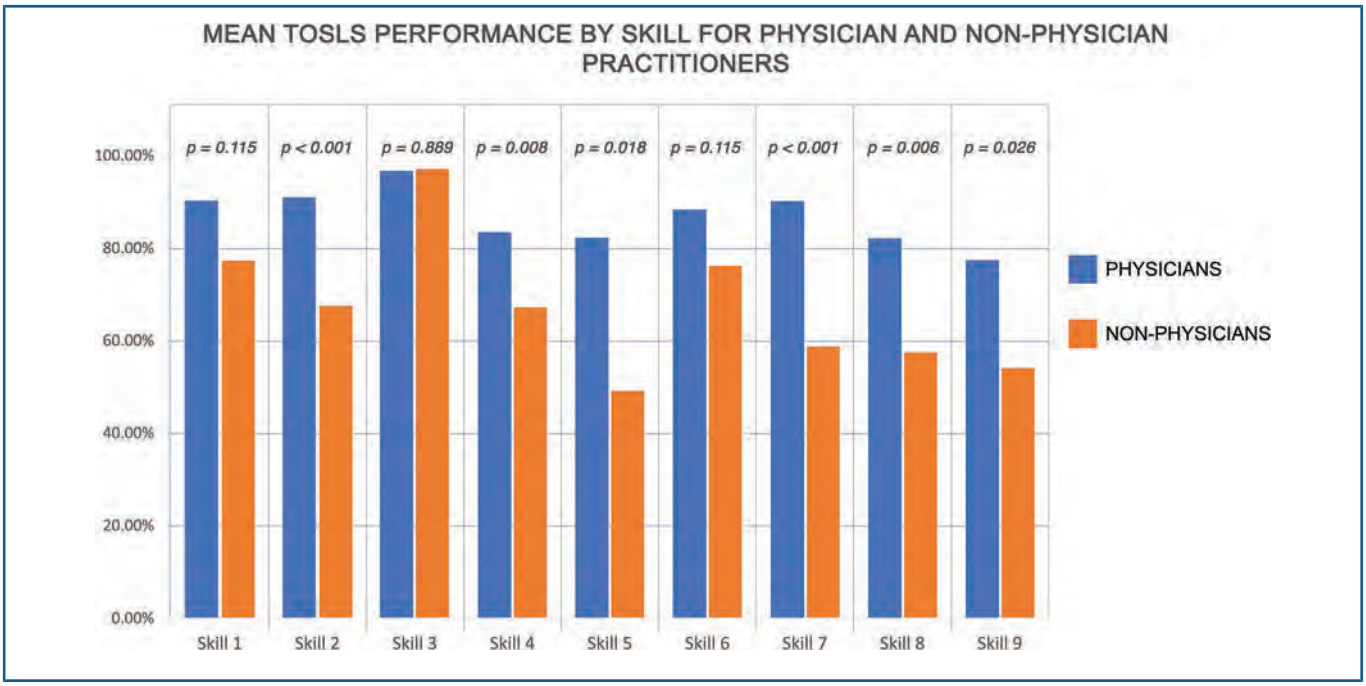


Figure 2. Skill-specific performance for physicians and nonphysicians on the test of scientific literacy skills.

Conclusion

The field of aesthetic medicine is rapidly evolving, with an influx of NPPs. This study indicates a pressing need for improved scientific literacy and evidence-based education among aesthetic medicine practitioners to ensure patient safety and promulgation of evolving care standards. The disparity in the medical literature engagement between physicians and nonphysicians highlights the necessity for educational structures that encourage continuous learning. The absence of a significant difference in clinical time dedicated to aesthetic medicine suggests that nonphysicians are integral to service delivery, emphasizing the need for standardized and comprehensive educational frameworks. By prioritizing scientific literacy and evidence-based practice, in a properly supervised clinical environment, the aesthetic medicine community can ensure that all practitioners are favorably positioned to provide the highest level of care.

References

1. Medical AMSPA. *Spa State of the Industry Report 2022*. Chicago, IL: American Med Spa Association; 2023. Available from https://americanmedspa.org/resources/med-spa-statistics. Accessed November 11, 2023.
2. Soares DJ, Yi CH, Bowhay A, Fakhre F, et al. The shifting face of aesthetic care: a systematic survey of medspa directorship and practitioner trends in Florida. *Plast Reconstr Surg* 2024. [In Review].
3. Wang JV, Albornoz CA, Noell C, Friedman PM, et al. Skewed distribution of medical spas and aesthetic physician practices: a cross-sectional market analysis. *Dermatol Surg* 2021;47:397–9.
4. Valiga A, Albornoz CA, Chitsazzadeh V, Wang JV, et al. Medical spa facilities and nonphysician operators in aesthetics. *Clin Dermatol* 2022;40:239–43.
5. Jalian HR, Jalian CA, Avram MM. Increased risk of litigation associated with laser surgery by nonphysician operators. *JAMA Dermatol* 2014;150:407–11.
6. Soares DJMD. Bridging a Century-Old Problem: the pathophysiology and molecular mechanisms of ha filler-induced vascular occlusion (FIVO)—implications for therapeutic interventions. *Molecules*. 2022; 27:5398.
7. Soares DJ, Bowhay A, Blevins LW, Patel SM, et al. Patterns of filler-induced facial skin ischemia: a systematic review of 243 cases and introduction of the FOEM scoring system and grading scale. *Plast Reconstr Surg* 2023;151:592e–608e.
8. Beleznay K, Carruthers JDA, Humphrey S, Carruthers A, et al. Update on avoiding and treating blindness from fillers: a recent review of the world literature. *Aesthet Surg J* 2019;39:662–74.
9. Zelickson Z, Schram S, Zelickson B. Complications in cosmetic laser surgery: a review of 494 Food and Drug administration manufacturer and user facility device experience reports. *Dermatol Surg* 2014;40:378–82.
10. Wang JV, Albornoz CA, Goldbach H, Mesinkovska N, et al. Experiences with medical spas and associated complications: a survey of aesthetic practitioners. *Dermatol Surg* 2020;46:1543–48.
11. FDA. Food and Drug Administration. *Executive Summary General Issues Panel Meeting on Dermal Filler*. Silver Spring, MD: FDA; 2021. Available from https://www.fda.gov/media/146870/download. Accessed November 11, 2023.
12. American Society for Dermatologic Surgery Association. *ASDSA Position Statement on Physician Oversight in Medical Spas*. Schaumburg, IL: American Society for Dermatologic Surgery Association; 2014. https://www.asds.net/Portals/0/PDF/asdsa/asdsa-position-statement-physician-oversight-in-medical-spas.pdf. Accessed November 11, 2023.
13. Carraccio C, Wolfsthal SD, Englander R, Ferentz K, et al. Shifting paradigms: from Flexner to competencies. *Acad Med* 2002;77:361–7.
14. Lee GSJ, Chin YH, Jiang AA, Mg CH, et al. Teaching medical research to medical students: a systematic review. *Med Sci Educ* 2021;31:945–62.
15. Kesten KS, Beebe SL. Competency frameworks for nurse practitioner residency and fellowship programs: comparison, analysis, and recommendations. *J Am Assoc Nurse Pract* 2021;34:160–8.
16. Kelley K, Clark B, Brown V, Sitzia J. Good practice in the conduct and reporting of survey research. *Int J Qual Health Care* 2003;15:261–6.
17. Pandis N, Fedorowicz Z. The international EQUATOR network: enhancing the quality and transparency of health care research. *J Appl Oral Sci* 2011;19
18. Gormally C, Brickman P, Lutz M. Developing a Test of Scientific Literacy Skills (TOSLS): measuring undergraduates' evaluation of scientific information and arguments. *CBE Life Sci Educ* 2012;11: 364–77.
19. Swing SR. Assessing the ACGME general competencies: general considerations and assessment methods. *Acad Emerg Med* 2002;9: 1278–88.
20. Mainiero MB, Lourenco AP. The ACGME core competencies: changing the way we educate and evaluate residents. *Med Health R* 2011;94:164–6.
21. Stanford Medicine. *Graduate Medical Education: Core Competencies*. Stanford, CA: Stanford Medicine; 2024. https://med.stanford.edu/gme/housestaff/current/core_competencies.html. Accessed November 11, 2023.
22. Soares DJ, Hynes SD, Yi CH, Shah-Desai S, et al. Cosmetic filler-induced vascular occlusion: a rising threat presenting to emergency departments. *Ann Emerg Med* 2023;S0196-0644:00578–4.
23. Arab K, Barasain O, Altaweel A, Alkhayyal J, et al. Influence of social media on the decision to undergo a cosmetic procedure. *Plast Reconstr Surg Glob Open* 2019;7:e2333.
24. He L, Chen Y, Xiong X, Zou X, et al. Does science literacy guarantee resistance to health rumors? The moderating effect of self-efficacy of science literacy in the relationship between science literacy and rumor belief. *Int J Environ Res Public Health* 2021;18:2243.

Original Article

Preventing and Treating Adverse Events of Injectable Fillers: Evidence-Based Recommendations From the American Society for Dermatologic Surgery Multidisciplinary Task Force

Derek H. Jones, MD,* Rebecca Fitzgerald, MD,† Sue Ellen Cox, MD,‡ Kimberly Butterwick, MD,§ M. Hassan Murad, MD,|| Shannon Humphrey, MD,¶ Jean Carruthers, MD,** Steven H. Dayan, MD,†† Lisa Donofrio, MD,‡‡ Nowell Solish, MD,§§ G. Jackie Yee, MD,||| and Murad Alam, MD¶¶

All injectable fillers may be associated with common injection site reactions such as redness, swelling, bruising, and tenderness, which usually resolve within 1 to 2 weeks. Rare but more serious adverse events from injectable fillers include vascular occlusion leading to skin necrosis or blindness, inflammatory events, and nodule formation, among others.[1] Although rare, they are likely underreported and increasing in frequency as the popularity of injectable fillers grows. Such adverse events can be distressing to both patient and physician and present therapeutic and potential legal challenges.[2] The American Society for Dermatologic Surgery (ASDS) has determined that the topic of preventing and treating these adverse events of injectable fillers requires the development of evidence-based clinical practice guidelines to support decision-making in daily practice.

*From the *Skin Care and Laser Physicians of Beverly Hills, Los Angeles, California; †Private Practice, Los Angeles, California; ‡Aesthetic Solutions, Assoc Clinical Faculty, UNC Department of Dermatology, Consulting Associate, Duke University Department Dermatology, Chapel Hill, North Carolina; §Cosmetic Laser Dermatology, San Diego, California; ||Evidence-based Practice Center, Mayo Clinic, Rochester, Minnesota; ¶Department of Dermatology and Skin Science, University of British Columbia, Vancouver, Canada; **Department of Ophthalmology and Visual Sciences, University of British Columbia, Vancouver, Canada; ††Denova Research, Clinical Assistant Professor, University of Illinois, Chicago, Illinois; ‡‡Department of Dermatology, Yale University School of Medicine, New Haven, Connecticut; §§Department of Dermatology, University of Toronto, Toronto, Canada; |||Baker Plastic Surgery, Miami, Florida; ¶¶Departments of Dermatology, Otolaryngology, and Surgery, Northwestern University, Chicago, Illinois*

D. H. Jones is an Investigator or Consultant for Allergan, Galderma, Merz and Revance. R. Fitzgerald is a Consultant for Allergan, Galderma, and Revance, and a Trainer for Galderma. S. E. Cox is Investigator and/or Consultant for Allergan, Croma, Evolus, Galderma, Merz and Revance. K. Butterwick is an Investigator or Consultant for Allergan, Galderma, Merz, Sinclair, Suneva, Histogen, Revance, and Evolus. M. H. Murad is a guideline methodologist with partial funding from ASDS to perform this work. S. Humphrey is a Consultant/Investigator/Speaker for Allergan, Galderma, and Revance, a Consultant/Speaker for Merz and L'Oreal, a Consultant for Sinclair Pharma, and an Investigator for Evolus. J. Carruthers is a Consultant and Investigator with Allergan, Alphaeon, Bonti, and Revance, and receives Royalties from Elsevier and UptoDate. S. Dayan is an Investigator or Consultant for Allergan, Galderma, Merz and Revance. L. Donofrio is a Consultant or Investigator for Canfield Scientific, Galderma, Allergan, and Revance. N. Solish is an Investigator or Consultant for Allergan, Galderma, Merz, Croma, and Revance. G.J. Yee is a Consultant for Allergan, Galderma, Revance, and Endo Aesthetics. The remaining author has indicated no significant interest with commercial supporters.

Address correspondence and reprint requests to: Derek H. Jones, MD, Skin Care and Laser Physicians of Beverly Hills, 9201 W. Sunset Boulevard, Suite 602, Los Angeles, CA 90069, or e-mail: derekjonesmd@gmail.com

http://dx.doi.org/10.1097/DSS.0000000000002921

Methods

American Society for Dermatologic Surgery convened a multidisciplinary task force that consisted of ASDS member physician specialists (8 board-certified in dermatology, 2 in plastic and reconstructive surgery, and 1 in oculoplastic surgery), 2 patient representatives, and a methodologist. The committee task force identified a priori 6 critical questions and commissioned the Mayo Clinic Evidence-based Practice Center to conduct systematic reviews to summarize the relevant evidence. These reviews are published separately.[3] The committee used the GRADE approach (Grading of Recommendations, Assessment, Development and Evaluation), which rates the certainty of evidence as high, moderate, low, or very low. Randomized trials start with a high certainty rating that can be lowered based on various factors and observational studies start with a low certainty rating that can be lowered or raised based on various factors.[4] The GRADE approach leads to 2 types of recommendations: (1) strong recommendations (most compelling, to be applied in most situations with minimal variation) that are denoted by the term "recommend," and (2) conditional recommendations (variation in care is acceptable based on the context and patient's values) that are denoted by the term "suggest." The determination of the strength of recommendation is based on the certainty of evidence, balance of benefits and harms, patient's values, resources, acceptability, and feasibility.[4]

Prevention of Vascular Occlusion, Blindness, and Stroke

Background

Accidental injection of filler into facial arteries can cause filler embolization and vascular occlusion, leading to tissue ischemia, necrosis, visual abnormalities, blindness, and stroke. Knowledge of vascular anatomy is essential for all filler injectors. Intravascular injection is possible at any injection location on the face, but certain locations carry a higher risk.

Recommendations

Although there is no absolutely risk-free injection protocol, ASDS Task Force recommends the following strategies to reduce the risk of vascular occlusion with injectable fillers (Strong recommendation, Moderate certainty evidence):

(1) Have a thorough knowledge of facial anatomy, blood vessels, and their cutaneous landmarks. Be aware that vascular variability may exist.
(2) Be aware of higher risk locations for blindness including the glabella, medial brow, nose, forehead, superior nasolabial fold, and medial tear trough
(3) Do not inject deep on preperiosteal planes in areas where arteries are located on bone, including the medial brow and glabella (supratrochlear and supraorbital arteries), medial canthus/tear trough (angular artery), medial cheek (infraorbital artery), and the antegonial notch of the jawline (facial artery)
(4) Strongly consider using a 25G blunt-tipped cannula or larger where possible
(5) Inject slowly with low plunger pressure, using small volumes with each pass, while keeping the cannula or needle moving
(6) Obtain pretreatment informed consent about the rare possibility of intravascular injection, tissue necrosis, blindness, stoke, and the emergent use of hyaluronidase.

Evidence and Rationale

The commissioned systematic review[3] included 3 comparative nonrandomized large studies and 18 noncomparative case series that fulfilled the specific inclusion criteria (a total of 7,318,824 patients who received mostly hyaluronic acid (HA) [84%] followed by calcium hydroxylapatite [10%]). The review focused on identifying risk factors such as the type and dose of the filler and injection technique.

From an anatomic perspective, the facial artery is a branch of the external carotid artery that crosses the jawline periosteally at the antegonial notch (just anterior to the anterior border of the masseter), and runs a deep, tortuous course from the lower lateral cheek to nasolabial fold, giving off branches to the inferior and superior labial arteries along the way, and becoming the angular artery near the superior border of the nasolabial fold (Figure 1). The angular artery then runs more superficially in a variety of patterns along the medial cheek and lateral nose[5] and then converges in an anastomotic intersection with 4 arteries: distal ophthalmic artery (with connections to the retinal and cerebral vasculature), supratrochlear and supraorbital arteries (branches of the distal ophthalmic artery, which cross periosteally over the supraorbital ridge beneath the medial brows and glabella and run superiorly through the forehead), and dorsal nasal artery along the nose. In order of risk, the nose, glabella, forehead, superior nasolabial fold, and medial cheek are considered high-risk zones for vascular occlusion and blindness,[6] although severe occlusion can occur at any injection location on the face, including the lips[7] (Figure 2A,B).

Blindness or visual compromise may very rarely occur if one of the above high-risk vessels is accidently cannulated and retrograde flow of filler occurs through the ophthalmic artery with embolization into the retinal artery. The most common areas of injection leading to blindness are the nose, glabella, forehead, and nasolabial folds.[6]

The ophthalmic artery is a branch of the internal carotid artery, which supplies the cerebral vasculature. End arteries of the ophthalmic artery may anastomose with branches of the external carotid artery such as the superficial temporal artery. Retrograde flow to the cerebral vasculature from such connections between the external and internal carotid artery system can rarely result in stroke and neurologic compromise.[6]

Needles and blunt-tipped cannulas both can perforate vessel walls. Larger 25G blunt-tipped cannulas, compared with smaller diameter cannulas and needles, have proven less likely to perforate vessels in cadaver models.[8] Surveys also suggest that intravascular occlusion is more common with needles.[7]

Injecting small volumes slowly and gently is recommended, because large volumes injected under high pressure may create more extensive occlusion in the case of accidental arterial injection. In addition, keeping the cannula or needle moving may reduce the likelihood of prolonged intravascular injection.

Retraction of the plunger on a syringe of HA filler (reflux test) is recommended before injection. Blood upon reflux indicates possible intravascular placement, indicating to immediately stop and reposition.[9,10] A negative reflux test does not definitively exclude intravascular placement.

Certainty in Evidence and Strength of Recommendation

The current recommendation depends on observational studies and basic anatomic and surgical principles in which we have higher certainty and can be considered best practice statements. Therefore, an overall moderate certainty rating was judged to be appropriate across the various strategies to reduce the risk of vascular occlusion with injectable fillers. This recommendation is strong and compelling because deviations from these surgical principles can lead to important complications. The panel, which included patient representatives, considered patient's values that emphasize avoidance of complications and other factors such as feasibility and acceptability of these preventive measures.

Implementation Techniques

Facial vascular anatomy should be studied in depth by all injectors. Cadaveric dissection courses and injection-related

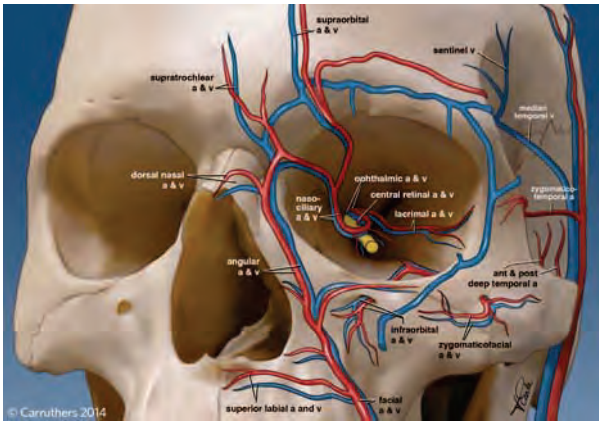


Figure 1. Vascular anatomy of the periocular region. Reproduced with permission from Carruthers and colleagues.[30]

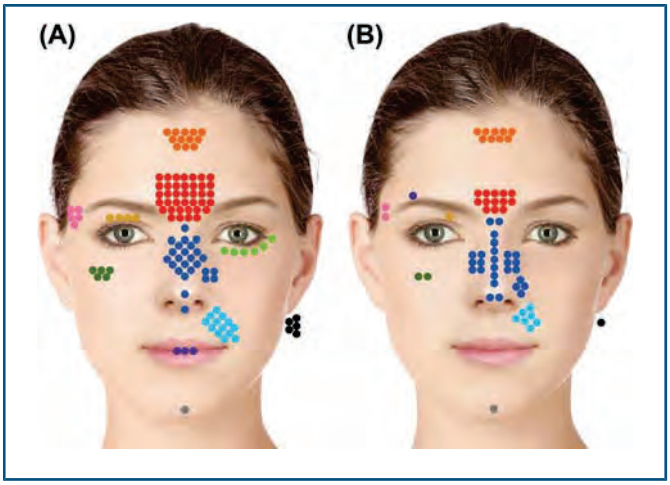


Figure 2. (A) Location of injection for each case of blindness from filler in 98 cases reviewed by Beleznay and colleagues.[23] Reproduced with permission. (B) Location of injection for each case of blindness from filler in 48 cases in an updated review by Beleznay and colleagues.[6] The black dots represent cases in which the location was not specified and listed as "face." Reproduced with permission.

vascular literature are recommended to learn the location and depth of major facial vessels.[11]

Although there is no completely risk-free injection protocol, the following are suggested as safer regional injection approaches:

Glabella, Nose, and Forehead

All 3 areas are high risk and should be approached with great caution only by the most experienced physician injectors. Do not inject deeply or on periosteum with needles or cannulas in the glabella, where supratrochlear and supraorbital arteries reside. Very experienced physicians may consider treating glabellar rhytides with superficial intradermal injections using small needles. The vasculature is variable, however, and may lie in a more superficial position.[12,13] Forehead reflation is considered safer with cannulas in the preperiosteal, subgaleal plane, 2 cm or more superior to the brow where the supratrochlear and supraorbital vessels run more superficially within the frontalis muscle.[14] Major vessels in the forehead run cephalad to caudal, and injections should be considered in the horizontal plane to avoid direct cannulization. Nasal injections represent the highest risk for blindness due to injection into the dorsal nasal artery. Cadaveric studies suggest that the safer plane of injection to the dorsal nose is preperiosteal or preperichondrial.[15] However, the vasculature is variable, and the dorsal nasal artery may lie on the periosteum in the midline.[16]

Temple

For reflation of the temple, the injection is deep to the superficial temporal vessels, on periosteum with a needle. The suggested safe zone is 1 cm up from the superior orbital rim, and 1 cm lateral to the temporal fusion line, and over 2.5 cm above the zygomatic arch to avoid the middle temporal vein.[17,18]

Cheeks and Nasolabial Fold

On the lateral cheek, periosteal injection with needle or cannula on the zygomatic prominence is generally considered safe, although the zygomaticofacial artery lies on periosteum, and a reflux test may be positive.[10] However, the medial cheek, medial to the midpupillary line, contains vessels that run periosteally (infraorbital vessels) and subcutaneously (variations of the angular artery) that are high risk. The facial artery runs deep in the submalar cheek, becoming the subcutaneous angular artery around the nasolabial fold. Although both needles and cannulas are FDA-approved in the medial cheek, submalar cheeks, and nasolabial folds, a 25G cannula or larger may be safer as cadaveric studies and reflux studies show the ability of needles to easily enter high-risk vessels in these areas.[7,8,10]

Lips

The labial arteries run deep to the wet dry line on the lips within the mucosa of the orbicularis oris. Injections should be superficial. The course of this artery has been recently reviewed.[19]

Chin and Jawline

Although periosteal injections appear safer on the inferior midline mandible to create chin projection and on the angle of the mandible to increase jaw width, care must be taken not to inject in a periosteal location along the mandibular ramus, just anterior to the anterior border of the masseter where the facial artery runs.[11]

Future Considerations

Cadaveric and imaging studies continue to enhance our knowledge of facial vascular anatomy.[11] Health care professionals should continue to study facial vascular anatomy in depth for the life of their career, with the understanding that it is invariably variable. Although there is no absolutely safe injection protocol, safer injection strategies may mitigate disastrous outcomes. The recent use of ultrasound in revealing vasculature may show promise.[20]

Treatment of Filler-Related Vascular Occlusion With Blindness

Background

Although the earliest reports of injection-related visual compromise (IRVC) were from autologous fat,[21–23] more recent reviews reveal an increase in HA-related cases.[6,24–27] This likely reflects the exponential increase in worldwide HA filler use.[28] Almost 200 unique cases of IRVC have been reported in the literature: 49% HA, 29% fat, and 22% from other fillers.[23–27,29] Although IRVC is rare, it is widely believed to be underreported.

Recommendations

The ASDS Task Force suggests the following strategies to reduce the risk of IRVC (conditional recommendation, low certainty evidence):

(1) Obtain informed consent from the patient regarding the rare possibility of IRVC, which can have life-altering consequences.

(2) Develop and post an IVRC protocol, review it with team members, and always have ample hyaluronidase on hand.

(3) Stop injecting at first sign of visual compromise, which usually occurs during or immediately after injection and is most often unilateral. Half of the patients show skin involvement, ophthalmoplegia, or ptosis, of which most resolve. Headache, nausea, and vomiting may or may not be present.

(4) Conduct evaluation of immediate postevent visual status BEFORE any intervention. The importance of this cannot be overstated.

- Document visual acuity in each eye separately and note in chart:

a. Ability to read letters (Snellen chart, near card, or magazine print)
b. Ability to count fingers
c. Ability to perceive hand motion
d. Light perception (LP)
e. No LP (NLP)

- Extraocular muscle function
- Pupillary response to light
- Photograph face in primary position

(5) Keep patient informed of evolving events, notify family member, and accompany both through entire process.

(6) In patients with signs or symptoms (s/s) of central nervous system (CNS) involvement, contact your local hospital's emergency stroke service and call 911 for immediate transport to the emergency room. In the absence of s/s, evaluate and image the patient to rule out CNS involvement once the ocular event has been addressed.

(7) Time is of the essence. Immediately contact an eye expert who is familiar with this risk and its management. A preexisting relationship with an oculoplastic surgeon, ophthalmologist, and/or retina specialist can avoid unnecessary delays.

(8) Hyaluronidase injections are quick, safe, and easily done at the bedside, and should be considered immediately. Inject >150 units hyaluronidase into the treated area, all areas of skin ischemia, and along the path of arteries leading to the eye. Similar doses can be injected adjacent to and in the supraorbital and supratrochlear foramina. Repeat in quick succession as needed. Retrobulbar (RBH) and peribulbar (PBH) injections may be beneficial, but this remains controversial at this time.

(9) Conservative measures that are quick, safe, and easily done at the bedside can be done simultaneously.

- Breathing into a paper bag (carbogen)
- Ocular massage. Manually press the globe firmly for cycles of 5 to 15 seconds intercalated by rapid release (rapid reperfusion may dislodge embolus), repeat for a total length of 5 minutes, rest (a few minutes), then repeat. This may be continued over hours.
- Topical Timolol and 500 mg oral acetazolamide to decrease intraocular pressure can be easily administered.

(10) Inform your indemnity malpractice carrier about the event as reporting requirements for coverage vary geographically. Keep detailed notes of events, interventions, and timing, and all interactions with patient, family, specialists, and facilities. Inform the product manufacturer of the incident for FDA reporting.

Evidence and Rationale

The commissioned systematic review[3] included 8 case series that fulfilled the specific inclusion criteria (a total of 96 patients who were treated for IRVC). Hyaluronidase injections were the main treatment used in the studies (retrobulbar, skin, and intralesional injections). Other treatments reported in these series were glucocorticoids, mechanical recanalization, urokinase injections, ocular massage, antiplatelet therapy, intraocular pressure lowering drugs and procedures, nitroglycerin, anticoagulants, and hyperbaric oxygen therapy. There were no comparative studies to provide reliable efficacy estimates for the various interventions. On the final evaluation, only 19% of the patients reported some degree of recovery from IRVC events.

From anatomical and physiologic standpoints, the leading hypothesis of HA IRVC pathogenesis involves inadvertent intra-arterial injection and retrograde flow of filler into the arterial supply of the eye (Figure 1).[21,23]

The treatment goal is to recanalize the occluded vessel(s) and reperfuse the tissue. IRVC is an ophthalmologic emergency. The most cited window of time for reperfusion is 90 minutes.[31] However, newer literature suggests it may be as little as 10 to 15 minutes, emphasizing the need for immediate recognition and a streamlined protocol.[32] The extent of visual compromise should be evaluated and documented before any intervention. The patient must be kept informed about the details of your treatment plan. Twenty percent of patients have CNS involvement necessitating emergent transfer to the hospital if any s/s are present.[6,23] A pre-existing relationship with an eye specialist familiar with this condition is an invaluable asset. British Eye Emergency Care Society survey data revealed that most of their specialist practitioners did not have local management guidelines for this complication (88%) nor were they aware of where to seek guidance to manage the complication (75%).[33] Plan accordingly and choose carefully. Litigation analysis commonly revealed deficiencies of informed consent.[2]

There is no current evidence-based standard of care for treating iatrogenic retinal embolism from HA filler. Kapoor's review of 44 cases from 2004 to 2019 using Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines was rated as level 3 evidence by the publishing journal.[34] Combined with a newly published case series of 24 patients from China,[27] these data comprise 70% (68/96) of the reported HA IRVC cases. Commonalities from these sources show the vast majority are from Asia, seen in young female patients, occur immediately after injection, and are unilateral. About half show skin involvement and/or ophthalmoplegia, from which most resolve.[34–36] Most cases involved injections in the nose,

glabella, and forehead. Temple, periorbital, and cheek accounted for the rest (Figure 2A,B).

Notably, cases involving the lower face (lip, chin, jawline) showed these patients were also injected in higher risk anatomic sites at the same session. No cases of HA IRVC were reported from the lower face when these areas were injected in isolation.[23,26,34]

Degree of vision loss predicts location of the embolus, which may be the most important prognostic factor. Partial vision loss after HA filler has a better prognosis than complete vision loss (Figure 3).[21,26,34]

Presentation with complete vision loss (NLP) is most often associated with ophthalmic artery occlusion (OAO) or central retinal artery occlusion (CRAO), and most do not recover.[21–23,34,37,38] Presentation with partial vision loss (blurry vision to diminished LP) is less commonly associated with OAO/CRAO, and more often includes more distal branches of both the posterior ciliary arteries or the central retinal artery, likely due to smaller emboli. Branch retinal artery occlusion (BRAO) has the most favorable prognosis.[26] Eighty percent of fat emboli present as complete vision loss, whereas 50% of HA present as partial vision loss, accounting for its better prognosis.[21,23,34]

All fully and partially recovered patients received some form of treatment.[6,34] The improvement rate was 42% (20/47) in those treated with hyaluronidase versus 33% (7/21) in those that did not receive hyaluronidase. Hyaluronidase degrades HA, affording a potential opportunity for vision rescue. The short therapeutic window and the ability to get the enzyme to the embolus are the challenges. Therefore, timing, dose, route of administration, secondary thrombosis, and perhaps the type of HA may all play a role. Kapoor found the nose, glabella, and forehead accounted for 85% of the cases.[34] These areas are supplied by the supraorbital, supratrochlear, and dorsal nasal arteries, which are terminal branches of the ophthalmic artery and therefore provide a direct path to the ocular circulation.[21,26,34] Because vascularity is often variable and the location of the embolus (or emboli) is unknown, it may be prudent to flood this entire area and the supraorbital and supratrochlear foramina with hyaluronidase.[39] High-dose hyaluronidase injected quickly at multiple sites (subcutaneous ± Foramina ± RBH) showed the most favorable results.[39–44] There are 7 reports of full recovery with the use of hyaluronidase.[39–44] PBH/RBH injections may be beneficial, but remain controversial awaiting further safety and efficacy data.[26,45,46] A favorable risk/benefit ratio may exist in cases of impending blindness when performed by a trained practitioner.[45] Cases treated with intra-arterial thrombolysis (IAT) using thrombolytics, hyaluronidase, or both, have heretofore reported disappointing results.[21,38,47] However, Zhang recently reported improvement in 10/24 cases (42%) using IAT with hyaluronidase ± urokinase, despite presentation with NLP/*LP* and delayed treatment.[29]

Traditional treatment for ocular occlusions not related to HA are aimed at lowering intraocular pressure with Timolol drops, acetazolamide, IV mannitol, or digital massage, dilating the retinal arteries (carbogen), decreasing edema (prednisone), and inhibiting thrombosis (aspirin).[21–23] Specialist treatments include anterior chamber paracentesis, direct intra-arterial or IV injection of hyaluronidase ±

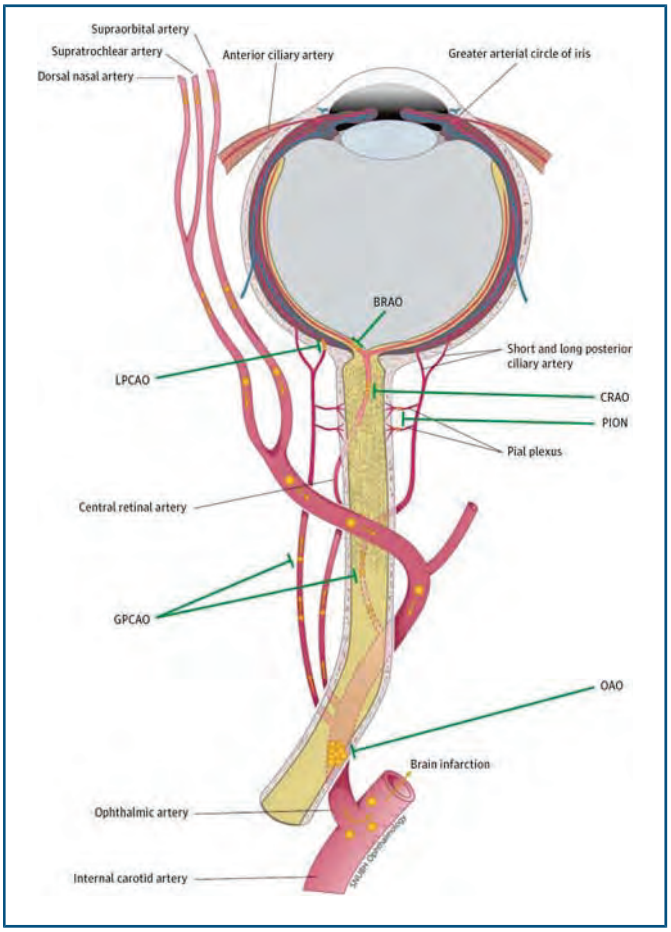


Figure 3. Schematic drawing of the ophthalmic artery, its branches, and possible obstruction points. Injected filler material (yellow droplet) is presumed to access the ophthalmic artery retrogradely via the supratrochlear, supraorbital, or dorsal nasal artery. Ophthalmic artery occlusion (OAO) is likely caused by complete proximal ophthalmic artery obstruction by a large filler bolus that migrated backward from the high injection pressure. It may also be that small particles migrated back to the central retinal artery and posterior ciliary artery origins and dispersed anterogradely into each branch as injection pressure decreased. This would cause a diffuse obstruction. Generalized posterior ciliary artery occlusion (GPCAO) or central retinal artery occlusion (CRAO) may occur depending on the extent of central retinal artery or posterior ciliary artery obstruction. When only the medial short posterior ciliary artery is involved, localized posterior ciliary artery occlusion (LPCAO) involving only the nasal choroid occurs. When only a branch of the central retinal artery is occluded, a branch retinal artery occlusion (BRAO) occurs. The mechanism of posterior ischemic optic neuropathy (PION) remains uncertain. The pial vascular plexus supplies blood to the intraorbital posterior optic nerve, and some vessels responsible for the pial plexus, which usually arise directly from the ophthalmic artery, may also be involved in these cases. Last, some particles may have accessed the internal carotid artery, causing a brain infarction. Reproduced with permission from Park and colleagues.[21]

urokinase for which isolated cases of improvement have been reported.[6,23] There are 2 reports of full recovery without the use of hyaluronidase. One was a BRAO who received 500 mg acetazolamide immediately; the other presented with a visual acuity of 20/20 and ophthalmoplegia who worsened to 20/200 with a field defect in 24 hours, then recovered after 14 days of conservative therapy.[48,49]

Certainty in Evidence and Strength of Recommendation

The current recommendation depends on uncontrolled observational studies and extrapolation from indirect evidence, case reports, and the panel's clinical experience. Therefore, the overall certainty rating was judged to be low. This recommendation is conditional. The panel, which included patient representatives, considered patient's values that emphasize avoidance of visual complications and other factors such as feasibility and acceptability of these preventive measures.

Implementation Techniques

Hypersensitivity reactions to hyaluronidase are uncommon but have been reported, mostly in the ophthalmology literature (0.05%), but not in the dermatology literature.[50] Patients with a history of anaphylactic reactions to bee stings may be more at risk.[50] Urgent situations may not allow time for skin testing. Video instructions for visual acuity testing and ocular massage can be found at (See **Supplemental Digital Content 1**, video, http://links.lww.com/DSS/A730).

Future Research

A registry to obtain the true number of cases and treatment details would be a valuable resource.[51] Information to further clarify the mechanism of action of this complication will guide techniques for prevention and treatment. Hyaluronidase ± thrombolytics may play a critical role in the treatment of HA IRVC, and further studies on the timing, dose, and route of administration (IAT, IV, RBH, OA injection) are needed, as is a more concentrated form of hyaluronidase to increase the dose without increasing the volume in some applications. Because this is a rare event, cadaveric and animal studies are invaluable.[52–54]

Treatment of Vascular Occlusion Without Blindness (Skin Ischemia)

Background

To reach areas that require tissue augmentation, needles or cannulas used to inject prepackaged soft tissue fillers into the deep dermis and subcutaneous tissues of the face often traverse densely vascularized areas, particularly those in the vicinity of the nose and mouth.[55–57] Veins or arteries may be inadvertently perforated such that filler material enters them, creating an obstruction that may impair vessel patency. It may be possible for the filler to accumulate adjacent to a vessel in sufficient quantity to cause tamponade and compromise blood flow. If not promptly recognized[58] and treated, either of these events, although infrequent,[59] can culminate in, successively, local tissue ischemia, necrosis, eschar and tissue slough, and permanent scar.

Recommendations

The ASDS task force recommends the strategies below for treatment of vascular occlusion (strong recommendation, moderate certainty evidence):

(1) During a patient filler injection, when vascular regurgitation in the syringe (i.e., "red flash") or tissue blanching in the treatment area is observed by the health care professional injector, the injection should be stopped and treatment with injectable hyaluronidase be considered.

(2) In patients who develop vascular occlusion of the skin of the face after treatment with filler, high-dose hyaluronidase should be injected promptly into the skin at the site of occlusion and any areas of ischemia on the immediate periphery.

Evidence and Rationale

The commissioned systematic review[3] included 8 case series that fulfilled the specific inclusion criteria (a total of 100 patients who were treated for vascular occlusion without blindness after the use of injectable fillers). Occlusive events were predominantly reported after receiving HA filler injections (97%). All of the included studies reported the use of hyaluronidase injections (including retrobulbar and skin injections) at a median time of 45 hours after developing vascular occlusion. The review did not identify any comparative studies. Across these series, 77% of the patients recovered from the vascular occlusive events (complete resolution of vascular occlusions without skin necrosis was achieved in 49% of the included cases).

A common surgical principle with supporting mechanistic evidence is that if blood enters the filler syringe when the needle tip is positioned at the point of injection and the plunger is retracted, this indicates that the needle tip is in a vessel lumen or has perforated a nearby vessel.[60] In this event, continuing to inject filler would increase the risk of vascular occlusion. Transient tissue blanching, or whitening, possibly in a reticulated pattern (i.e., livedoid), and lasting a few seconds or longer, has also been noted to be an indicator of vascular compromise due to filler injection. When observed, this blanch typically occurs immediately after the filler is injected. Patient-reported pain, asymmetric edema, and slow capillary refill may help confirm the diagnosis.[61]

Since 1971, it has been known that hyaluronidase is effective for catalyzing the disintegration of HA, the principal constituent of HA fillers. Among the FDA-approved formulations of hyaluronidase are those that are animal-derived (Hydase and Vitrase) and human recombinant (Hylenex). Of all the measures that can be undertaken to reverse an unwanted accumulation of HA filler in or around a vessel, hyaluronidase injection is the most specific and also the only intervention supported by virtually unanimous expert consensus.[62–72] Hyaluronidase is believed to be effective in this context by dissipating the HA

filler both in the vessel lumen and encircling the vessel. Although there is a lack of consensus regarding the optimal dosage of hyaluronidase, which may vary based on clinical circumstances and the particular HA formulation, there is consensus that total dosage at each point in time hyaluronidase is injected should be on the order of hundreds of units.

Certainty in Evidence and Strength of Recommendation

Reliance on signs such as "red flash" or tissue blanching is supported by physiologic and anatomic principles and likely reflects high certainty evidence. The certainty of evidence supporting the effectiveness of injectable hyaluronidase is of lower certainty and is based primarily on observational studies. However, the strong recommendation for its use as a treatment after a vascular occlusion has occurred is based on patient's values that emphasize avoidance of complications and other factors such as safety, feasibility, and acceptability of using hyaluronidase.

Implementation Techniques

Hyaluronidase injections are likely to be most useful in reversing a skin vascular occlusion and preventing tissue necrosis if they are delivered immediately after occlusion. In addition, since the half-life of hyaluronidase in the skin is counted in minutes, repeat injections should be considered. A recent study by Lee and colleagues[63] found superior results when 500 units was administered as 125 units at 15-minute intervals rather than as a single bolus. Unfortunately, vascular occlusions of the skin are often not detected at the time of injection, instead being discovered when the patient reports persistent pain, swelling, or redness 1 or 2 days later.[73] Because office staff may receive the relevant call from an affected patient, identification of the problem may be contingent on nurses and other office staff being educated[51] that such sequelae require further investigation, ideally with the patient coming to the office for a clinical examination.

Apart from hyaluronidase injections, skin massage, intralesional or systemic corticosteroids, warm compresses, and oral aspirin may be helpful in treating skin vascular occlusion. The expert panel noted that nitroglycerin may be less useful.[74–76] If a calcium hydroxylapatite filler is responsible for an occlusion, there is early evidence that sodium thiosulfate injection may dissipate the filler,[77,78] although evidence is lacking regarding its use with vascular occlusion. By 1 to 2 days after occlusion onset, necrosis may not be preventable.[79,80] At this point, management consists of wound care, including appropriate topical emollients and wound dressings. Antimicrobials, such as antibiotics or antivirals, may be considered if there is evidence of incipient infection in devitalized skin, and hyperbaric oxygen treatments have been attempted.[81] Once the site has healed, the need for scar revision is evaluated.

Reducing the risk of skin vascular occlusions may be possible. There is an emerging consensus that filler injection with cannulas,[82] particularly those of higher bore, may be less likely to injure vessels than injection with needles. Slow, superficial, and low volume injections, and injections that aim upward, tenting the skin, may also reduce risk, although these common-sense strategies have not been well-studied.

Future Research

Research is needed to better understand the pathophysiology of vascular skin occlusions associated with filler injections. Animal studies may be appropriate to characterize the scale and loci of anatomic disruptions, which may clarify the optimal doses of hyaluronidase needed and also provide insight into injection methods that reduce the risk of intravascular injection.

Reducing the Incidence of Nodules With Hyaluronic Acid Fillers

Background

Nodules can develop with injections of all iterations of HA soft tissue fillers.[1,83] For the purposes of these ASDS evidence-based guidelines, we define nodules as early or late onset events (late presenting more than 4 weeks post-treatment) and as either inflammatory (erythematous, edematous, tender, hot) or noninflammatory (nontender, minimal erythema). Delayed-onset adverse reactions of over 1-month duration are uncommon, but with the advent of newer fillers and increased popularity of injectable soft tissue augmentation, more reports of such events are found in the literature.[83] In addition, delayed nodules because of certain HA fillers manufactured with Vycross technology have been found in some reports to have a higher incidence of late-onset nodules.[84–87] Prevention strategies are therefore needed.

Recommendations

The ASDS task force recommends active adoption of strategies to reduce the risk of inflammatory and noninflammatory early and late nodules (strong recommendation, low certainty evidence):

(1) Obtain a thorough history regarding active facial infection, autoimmune diseases, recent dental work, immunizations, facial trauma, and past history of permanent or non-HA fillers
(2) Avoid injection into areas with active inflammation
(3) Adopt aseptic technique
(4) Use the smallest bolus possible, such as 0.1 to 0.2 mL.
(5) Provide post-treatment patient education including delaying application of make-up, creams, lotions, tap water, ice, and avoiding manipulation of the area after the procedure
(6) Avoid dental procedures, invasive diagnostic procedures, and surgical procedures for greater than 2 weeks either before or after filler procedures

Evidence and Rationale

The commissioned systematic review[3] included 41 randomized controlled trials, 6 comparative observational studies, and 81 noncomparative case series that reported on a total of 6,183,147 patients who received different brands of HA filler injections for aesthetic purposes. The review also

included a separate analysis with a total of 2,537 nodules and inflammatory events related to HA injections reported to the FDA MAUDE database over a 10-year period (2007–2017). The review focused on identifying risk factors such as the type and dose of the filler and injection technique.

The overall safety profile of HA fillers is very good. Adverse events are rare based on the number of worldwide injectable procedures. Delayed-onset adverse event reactions are uncommon and consist of both cyclic and persistent areas of facial edema, erythema, tenderness and firm nodules, or indurated plaques. The underlying etiology may involve either the manufacturing process or nature of the product, host sensitivity, injection technique, or a combination of these factors. Inflammatory nodules may stem from systemic immune up-regulation, hypersensitivity, foreign body reaction, infection, sterile abscess, or biofilm.[88–90] Noninflammatory cold nodules may be due to inadvertent placement superficially, migration, or excessive product. Host factors include immune sensitivity, prior permanent fillers, and systemic or active infection. Some series have demonstrated an increased risk of delayed nodules after a flu virus,[85] after vaccinations or immunizations,[91] and during cold and flu season.[92] Regarding the type of HA, 3 separate studies indicated that Vycross technology has a 1% to 4% delayed nodule risk, which may be related to the area injected (lips, tear trough).[86,87,92] Although unclear, lower molecular weight oligosaccharides in Vycross may be immunogenic. Hypersensitivity has been most associated with delayed-onset nodules, but biofilms and atypical organisms have been implicated in some cases.[88,89] Aseptic technique is encouraged, although clinical evidence has failed to prove that one technique is better than another.[91,93,94] There is a lack of consensus regarding the period of time to resume make-up application and avoid tap water exposure, although most suggest a delayed period of time after the filler session.[84]

Certainty in Evidence and Strength of Recommendation

The current recommendation depends on observational studies and basic anatomic and surgical principles in which we have higher certainty and can be considered best practice statements. The evidence supporting strategies and interventions to reduce the risk of nodules after injection is however of low certainty. The panel, which included patient representatives, considered patient's values that emphasize avoidance of nodules and other factors such as feasibility and acceptability of these preventive measures.

Implementation Techniques

A thorough patient history is essential. Aseptic technique is an important preventative factor. Patients must have a clean, make-up free face before injections. Alcohol alone may not be sufficient. Antiseptic cleansers such as chloroxylenol, benzalkonium chloride, hypochlorous acid, or povidone iodine should be considered. Avoid touching the cannula during treatment, and change needles frequently. Larger injection quantities may contribute to an increased level of risk.[92] Specific types of fillers such as HAs with Vycross technology have been associated with increased risk. Patients should be advised to avoid potential triggering factors (dental procedures, vaccinations, manipulation) for a period of 2 weeks or longer following HA filler injections.

Future Research

Research is needed to better understand the differences in injectable fillers, specifically why certain crosslinking technology such as Vycross with both high and low molecular weight particles seems to be more immunogenic. More evidence-based data on prevention, aseptic technique, and treatment is necessary. In addition, a central repository to collect these types of complications is crucial.

Treatment of Nodules and Inflammatory Events From Hyaluronic Acid Fillers

Background

Hyaluronic acid fillers have become the most versatile and widely used subset of volumizing fillers worldwide. Inflammatory and noninflammatory nodules due to HA filler injections are uncommon, but there are a number of reports of nodule formation due to all HA fillers.[1] Early nodules (developing <4 weeks after implantation) may be common treatment responses that usually resolve, or related to injection technique (too superficial, excessive amount, incorrect anatomical area) and are reversible with hyaluronidase. Late-onset nodules (developing >4 weeks after implantation) have been increasingly reported in the past 5 years,[85,86,92] and their diagnoses and management are often challenging.

Recommendations

The ASDS task force suggests the following measures to manage inflammatory and noninflammatory early and late nodules (conditional recommendation, low certainty evidence):

(1) Differentiate between noninflammatory (firm, nontender, no erythema) and inflammatory (erythematous, edematous, tender).
(2) Noninflammatory nodules caused by overcorrection or superficial placement that are persistent and bothersome may be treated with intralesional hyaluronidase
(3) For inflammatory nodules, rule out possible infection by history and examination (warmth, drainage, fluctuance, severe induration, tenderness, erythema, or fever)
   - If fluctuant, incision, drainage, and appropriate stains and cultures are recommended.
(4) If infection is suspected, broad-spectrum antibiotic therapy should be instituted and modified as cultures dictate. Dual antibiotic therapy should be instituted if a triggering event is suspected (sinusitis, dental abscess, other) or if the nodule(s) persists, with consideration of a quinolone and macrolide.
(5) Delayed noninflammatory nodules without suspicion of infection may be treated initially with oral corticosteroids for 1 to 2 weeks, rather than dissolving with hyaluronidase, should the retention of the filler effect be desired. Addition of antibiotics

(doxycycline or minocycline) should be considered for anti-inflammatory and antimicrobial properties.

(6) Alternatives to a course of oral corticosteroid therapy include intralesional triamcinolone with or without 5-fluououracil (5-FU), or intralesional hyaluronidase.

Evidence and Rationale

The commissioned systematic review[3] included 6 case series of inflammatory events and 14 of nodules that were treated with hyaluronidase injections (total of approximately 300 patients). The overwhelming majority of these events were of late-onset (≥1 month). The reported resolution rates were 80% and 78%; respectively. Other interventions administered in the series included conservative management, saline dressings, probiotics, antibiotics, antihistamines, hydroxychloroquine, oral valacyclovir, ibuprofen, indomethacin, corticosteroids, drainage, and surgery. There were no comparative studies to derive true efficacy estimates for the various interventions. Therefore, this recommendation is based on case reports and adverse events noted in large retrospective analyses[92] and randomized clinical trials[95]; and input of the ASDS task force about how they treat adverse events in their own practice.

Optimal treatment depends on appropriate diagnosis of noninflammatory versus inflammatory nodules[92,96] and whether an infectious process is suspected.[90,96] Severity and associated symptoms of the nodule also play a role in its management. Early nodules (<4 weeks from implantation) due to HA are most likely because of technique or inappropriate product for the area and may be efficiently treated with reassurance or dissolved with hyaluronidase depending on severity. Some HA fillers are more difficult to dissolve and may require increased doses of hyaluronidase for complete resolution.[97,98] Delayed-onset nodules (>4 weeks from implantation) are often likely immune-mediated, but may be infectious.[83,92] It is important to first rule out and/or treat active acute infectious processes, obtain cultures and treat with antibiotics if infection is suspected. Without s/s of active infection (fluctuance, heat, associated adjacent or concomitant systemic infection), oral corticosteroids have proven effective, particularly with Vycross-associated nodules.[92]

Dosing protocols vary, ranging from 1 to 2 weeks of therapy with or without tapering and repeating the course of corticosteroids, should the nodule recur, with an average starting dose of 30 mg of prednisone per day. Intralesional triamcinolone acetonide may be considered if oral steroids are contraindicated or declined. Concomitant treatment with doxycycline or minocycline should considered as well for antimicrobial and anti-inflammatory effects. In cases resistant to treatment with cortisone and antibiotics, hyaluronidase in appropriate doses depending on the filler may be instituted. Products using Vycross technology prove harder to dissolve, and larger doses may be necessary, with hundreds of units of hyaluronidase needed to dissolve 1 cc of Vycross gels.[98] Biofilms may play a role in resistant cases although a cause and effect role has not been proven.[90] Intralesional 5-FU (50 mg/mL) in combination with triamcinolone may be helpful for stubborn cases as 5-FU has been well documented to have both antimitotic and antimicrobial effects.[88]

Certainty in Evidence and Strength of Recommendation

The current recommendation depends on observational studies of low certainty. The panel considered patient's values that emphasize great desire to resolve nodules and other factors such as feasibility and acceptability of the recommended treatments.

Implementation Techniques

Expert consensus is that not all nodules require treatment. Early-onset nodules are often related to placement of the material or injection responses that frequently resolve with time. Some late-onset nodules may resolve spontaneously without treatment and can be followed clinically.[92] Treatment options for noninflammatory delayed nodules include 30 mg of prednisone given by mouth in the morning for 1 to 2 weeks in combination with doxycycline or minocycline. Alternatives include intralesional triamcinolone with or without 5-FU (see implementation section under non-HA and permanent fillers for more information). For unresponsive or recurrent delayed nodules, hyaluronidase is effective in proper doses. Vycross technology may take hundreds of units to dissolve 1 cc of gel. Fluctuant, warm nodules should be approached differently, with the consideration for an infectious etiology that would require incision and drainage, bacterial culture, and antibiotic therapy. Biopsy is rarely needed, because clinical correlation can be sufficient to make the diagnosis but may be useful in resistant cases, especially where prior placement of permanent fillers is suspected.

Future Research

Comparative studies with different management protocols would be invaluable but may be impractical because of the relatively small numbers of cases per institution. Therefore, prospective patient registries and multicenter collaborations are needed. Further understanding etiology of delayed nodules and optimal dosing for corticosteroid therapy and hyaluronidase is needed.

Treatment of Nodules Caused From Permanent and Semipermanent Fillers

Background

Nodules and induration are more common with the permanent fillers liquid injectable silicone (LIS) and polymethylymethacrylate (PMMA) (Bellafill, Suneva Medical, San Diego, CA and others outside the US).[90,99–101] They appear years after injection and are usually granulomatous on biopsy. Non FDA-approved hydrogel polymers polyakylimide (Bio-Alcamid, Polymekon, Brandisi, Italy) and polyacrylamide (Aquamid, Soeburg, Denmark, and others outside the US) are prone to late-appearing abscesses that may be infectious and drainable.[90,102–106] Semipermanent fillers include poly-L-lactic acid (PLLA) (Sculptra,

Restylane fillers; Galderma, Uppsala, Sweden) and calcium hydroxylapatite (CaHa) (Radiesse, Belotero fillers; Merz, Franksville WI), which are not permanent but induce fibroplasia over time. Both may cause nodules that may be granulomatous on biopsy.[107,108] Occasionally, nodules may occur because of overcorrection, excessive fibroplasia, or misplacement of product too superficially or in inappropriate anatomical areas. Unfortunately, in most cases there is no erasing agent to eradicate these fillers, as is possible with hyaluronidase for HA fillers (with the possible exception of sodium thiosulfate for CaHa).[77,78]

Recommendations

The ASDS task force suggests the following measures to manage nodules caused from permanent and semipermanent fillers (conditional recommendation, low certainty evidence):

(1) In patients presenting with nodules after skin fillers, identification of the filler responsible for the nodule is important because filler type can affect the choice of treatment. If history is not reliable, we suggest a biopsy or ultrasound.
(2) In patients with "hot" nodules that are red, tender, edematous, indurated, and warm, antibiotic therapy that covers common skin pathogens (staphylococcus aureus, streptococcal species, p. acnes) may be considered.
(3) In patients with fluctuant nodules, incision, drainage, and cultures are recommended.
(4) In patients with "cold" nodules (not red, tender, warm, or fluctuant) caused by LIS or PMMA, intralesional injections of 5-FU mixed with triamcinolone at monthly intervals are recommended. Laser therapies may be considered for those who fail intralesional injections.
(5) In patients with nodules after hydrogel polymers (Bioalcamid, Aquamid) who are more prone to late-appearing fluctuant abscesses, incision and drainage of the filler, with antibiotics to cover streptococcus viridans in addition to common skin pathogens are recommended.
(6) In patients with nodules caused from PLLA, watchful waiting is recommended because these nodules usually resolve over months to years without treatment. Injections with triamcinolone with or without 5-FU may be useful for troublesome nodules where watchful waiting is not acceptable.
(7) Nodules from CaHa usually resolve over months to years without treatment. For troublesome nodules where watchful waiting is not acceptable, intralesional injection of aqueous solutions with vigorous massage, and consideration of sodium thiosulfate are recommended.
(8) Surgical excision is considered a last resort

Evidence and Rationale

The commissioned systematic review[3] included 22 noncomparative case series totaling 333 patients who were treated for inflammatory events related to different types of permanent and semipermanent dermal fillers. Resolution of filler-related inflammatory events after receiving an intervention was achieved in 86% of the patients. Most of the cases were late-onset (≥1 month). Patients who underwent treatment for early-onset inflammatory events (<1 month) had a 100% success rate. Interventions used in this series included massage, ice compresses, non steroidal anti inflammatory medications (NSAIDs), corticosteroids, antibiotics, laser therapy, needle aspiration, incision and drainage, and surgery. Data were inadequate to draw conclusions about the efficacy of different interventions. The review also identified 25 noncomparative case series totaling 684 patients who were treated for nodules related to permanent and semipermanent dermal filler injections. Resolution of nodules after receiving an intervention was achieved in 77% of the patients; most of which were of late-onset nodules (≥1 month). Interventions used in this series include massage, NSAIDs, corticosteroids, antibiotics, hydroxychloroquine, laser therapy, needle aspiration, incision and drainage, and surgery. Data were inadequate to draw conclusions about the efficacy of the various interventions.

In patients presenting with nodules after injectable fillers, identification of the filler responsible for the nodule is essential, as the filler type will affect the choice of treatment, especially with non-HA fillers. If history is not reliable, biopsy or ultrasound may offer guidance.[20,109,110]

Most nodules caused by LIS and PMMA appear years after injection. Nodules are usually foreign body granulomas on biopsy and respond to injection with intralesional triamcinolone.[99] There are reports of successfully treating PMMA and other permanent filler nodules with laser.[111,112] Many nodules caused by fillers (permanent or non-permanent) are labeled biofilms. Biofilms are complex colonies of bacteria that adhere to surfaces and are resistant to antibiotics and difficult to culture. Although there is insufficient evidence proving that biofilms are causative of filler nodules, it is prudent to consider antimicrobial therapy. Some protocols recommend 2 weeks of double antibiotic therapy (a macrolide and quinolone),[90] but efficacy data are lacking. There is solid evidence that 5-FU has potent antimicrobial properties, in addition to antimitotic properties.[88,113] Monthly intralesional injection of lower doses of triamcinolone admixed with 50 mg/cc 5-FU has proven effective for delayed nodules from LIS and may decrease the risk of adverse events associated with higher doses and concentrations of triamcinolone, while adding the antimicrobial properties of 5-FU.[100] However, nodules or induration may reappear over months to years, necessitating reinjection.

Hydrogel polymers consist of over 95% water and a small percentage of the synthetic polymers polyalkylamide (Bio-Alcamid) or polyacrylamide (Aquamid). Both are associated with late-appearing infections, and antimicrobial therapy should be used when treating nodules or abscesses. In 2 publications reporting a total of 19 cases of late-appearing abscesses to Bio-Alcamid, most resolved with incision and drainage, with and without irrigation. Cultures revealed streptococcus species in the majority, particularly streptococcus viridans, which underscores the recommendation to use antibiotics covering streptococcus species in these cases.[102,104] Nondrainable nodules without fluctuance may be treated with broad-spectrum oral antibiotics and intralesional 5-FU and triamcinolone.

Nodules related to PLLA are often granulomatous on biopsy[107,108] and may be treated with intralesional

cortisone with or without 5-FU. Nodules will often spontaneously resolve over months to years.

Nodules related to CaHa also often spontaneously resolve over months to years. Injections of aqueous solutions combined with massage may also help disperse CaHa nodules.[114] Early evidence is promising using intralesional sodium thiosulfate to eradicate CaHa in vivo to resolve nodules, but it requires further study to determine efficacy and safety.[77,78]

For all nodules caused by permanent and semipermanent fillers, excision is a last resort.

Certainty in evidence and strength of recommendation

The current recommendation depends on observational studies of low certainty. The panel considered patient's values that emphasize great desire to resolve nodules and other factors such as feasibility and acceptability of the recommended treatments.

Implementation Techniques

Where indicated as an intralesional treatment, 5-FU is supplied as a 50 mg/cc solution. One long-term study has achieved good results treating LIS nodules with 1 cc of 50 mg/cc 5-FU admixed with 0.1 cc of 40 mg/cc triamcinolone and injected intralesionally into the nodule.[100] Superficial intradermal injections should be avoided to prevent atrophy. It is recommended not to exceed 2 cc's of this mixture during a single treatment to avoid systemic toxicity. Treatments are performed at monthly intervals until optimal resolution is achieved. For all nodules, the ASDS task force suggests excision as a last resort, where other treatment modalities have failed.

Future Research

Future research is needed to define the role of biofilm and immune system triggers in the etiology of nodules caused from permanent and semipermanent fillers, and the role of antimicrobial and immune suppressant therapies. Further research is also needed to elucidate the safety and effectiveness of sodium thiosulfate for CaHA nodules, and to develop more proven treatment protocols.

Acknowledgments

Editorial support was provided to the authors by Diane K Murphy, MBA, and was funded by ASDS.

References

1. Povolotskiy R, Oleck NC, Hatzis CM, Paskhover B. Adverse events associated with aesthetic dermal fillers: a 10-year retrospective study of FDA data. *Am J Cos Surg* 2018;35:143–51.
2. Rayess HM, Svider PF, Hanba C, Patel VS, et al. A cross-sectional analysis of adverse events and litigation for injectable fillers. *JAMA Facial Plast Surg* 2018;20:207–14.
3. Nayfeh T, Shah S, Malindras K, Amin M, et al. A systematic review supporting the American Society for Dermatologic Surgery guidelines on the prevention and treatment of adverse events of injectable fillers. *Dermatol Surg* 2021;47:227–34.
4. Murad MH. Clinical practice guidelines: a primer on development and dissemination. *Mayo Clin Proc* 2017;92:423–33.
5. Kim YS, Choi DY, Gil YC, Hu KS, et al. The anatomical origin and course of the angular artery regarding its clinical implications. *Dermatol Surg* 2014;40:1070–6.
6. Beleznay K, Carruthers JDA, Humphrey S, Carruthers A, et al. Update on avoiding and treating blindness from fillers: a recent review of the world literature. *Aesthet Surg J* 2019;39:662–74.
7. Goodman GJ, Roberts S, Callan P. Experience and management of intravascular injection with facial fillers: results of a multinational survey of experienced injectors. *Aesthet Plast Surg* 2016;40:549–55.
8. Pavicic T, Webb KL, Frank K, Gotkin RH, et al. Arterial wall penetration forces in needles versus cannulas. *Plast Reconstr Surg* 2019;143:504e–512e.
9. Fitzgerald R, Bertucci V, Sykes JM, Duplechain JK. Adverse reactions to injectable fillers. *Facial Plast Surg* 2016;32:532–55.
10. Tseng FW, Bommareddy K, Frank K, DeLorenzi C, et al. Descriptive analysis of 213 positive blood aspiration cases when injecting facial soft tissue fillers. *Aesthet Surg J*. 2020;sjaa075. doi:10.1093/asj/sjaa075. Epub 2020 Jun 6.
11. Cotofana S, Lachman N. Arteries of the face and their relevance for minimally invasive facial procedures: an anatomical review. *Plast Reconstr Surg*. 2019;143:416–26. Erratum in: Plast Reconstr Surg. 2019;143(4):1282-1283.
12. Cho KH, Dalla Pozza E, Toth G, Bassiri Gharb B, et al. Pathophysiology study of filler-induced blindness. *Aesthet Surg J* 2019;39:96–106.
13. Cotofana S, Alfertshofer M, Frank K, Bertucci V, et al. Relationship between vertical glabellar lines and the supratrochlear and supraorbital arteries. *Aesthet Surg J*. 2020;sjaa138. doi:10.1093/asj/sjaa138. Epub 2020 May 29.
14. Carruthers JDA, Carruthers JA. Appreciation of the vascular anatomy of aesthetic forehead reflation. *Dermatol Surg* 2018;44:S2–S4.
15. Choi D, Bae J, Youn K, Kim W, et al. Topography of the dorsal nasal artery and its clinical implications for augmentation of the dorsum of the nose. *J Cosmet Dermatol* 2018;17:637–42.
16. Lee W, Kim JS, Oh W, Koh IS, et al. Nasal dorsum augmentation using soft tissue filler injection. *J Cosmet Dermatol* 2019. doi:10.1111/jocd.13018. Epub 2019 Jun 3.
17. Carruthers J, Humphrey S, Beleznay K, Carruthers A. A suggested injection zone for soft tissue fillers in the temple. *Dermatol Surg* 2017;43:756–7.
18. Cotofana S, Gaete A, Hernandez CA, Casabona G, et al. The six different injection techniques for the temple relevant for soft tissue filler augmentation procedures—clinical anatomy and danger zones. *J Cosmet Dermatol* 2020;19:1570–9.
19. Cotofana S, Alfertshofer M, Schenck TL, Bertucci V, et al. Anatomy of the superior and inferior labial arteries revised: an ultrasound investigation and implication for lip volumization. *Aesthet Surg J*. 2020;sjaa137. doi: 10.1093/asj/sjaa137. Epub 2020 May 29.
20. Schelke LW, Decates TS, Velthuis PJ. Ultrasound to improve the safety of hyaluronic acid filler treatments. *J Cosmet Dermatol* 2018;17:1019–24.
21. Park KH, Kim YK, Woo SJ, Kang SW, et al. Iatrogenic occlusion of the ophthalmic artery after cosmetic facial filler injections: a national survey by the Korean Retina Society. *JAMA Ophthalmol* 2014;132:714–23.
22. Chen Y, Wang W, Li J, Yu Y, et al. Fundus artery occlusion caused by cosmetic facial injections. *Chin Med J (Engl)* 2014;127:1434–7.
23. Beleznay K, Carruthers JD, Humphrey S, Jones D. Avoiding and treating blindness from fillers: a review of the world literature. *Dermatol Surg* 2015;41:1097–117.
24. Sorensen EP, Council ML. Update in soft-tissue filler-associated blindness. *Dermatol Surg* 2020;46:671–7.
25. Chatrath V, Banerjee PS, Goodman GJ, Rahman E. Soft-tissue filler-associated blindness: a systematic review of case reports and case series. *Plast Reconstr Surg Glob Open* 2019;7:e2173.
26. Lee W, Koh IS, Oh W, Yang EJ. Ocular complications of soft tissue filler injections: a review of literature. *J Cosmet Dermatol* 2020;19:772–81.
27. Zhang LX, Lai LY, Zhou GW, Liang LM, et al. Evaluation of intraarterial thrombolysis in treatment of cosmetic facial filler-related ophthalmic artery occlusion. *Plast Reconstr Surg* 2020;145:42e–50e.

28. International Society of Aesthetic Plastic Surgery. *ISAPS Global Statistics*. Available from: https://www.isaps.org/medical-professionals/isaps-global-statistics. Accessed March 17, 2020.
29. Abtahi-Naeini B, Pourazizi M, Saffaei A. Systematic review of soft-tissue filler-associated blindness: a methodologic concern beyond duplicated cases. *Plast Reconstr Surg Glob Open* 2019;7:e2380.
30. Carruthers JD, Fagien S, Rohrich RJ, Weinkle S, et al. Blindness caused by cosmetic filler injection: a review of cause and therapy. *Plast Reconstr Surg* 2014;134:1197–201.
31. Hayreh SS, Zimmerman MB, Kimura A, Sanon A. Central retinal artery occlusion. Retinal survival time. *Exp Eye Res* 2004;78:723–36.
32. Tobalem S, Schutz JS, Chronopoulos A. Central retinal artery occlusion—rethinking retinal survival time. *BMC Ophthalmol* 2018;18:101.
33. Joganathan V, Shah-Desai S. Awareness of management of hyaluronic acid induced visual loss: a British National Survey. *Eye (Lond)*. 2020;34:2280–2283.
34. Kapoor KM, Kapoor P, Heydenrych I, Bertossi D. Vision loss associated with hyaluronic acid fillers: a systematic review of literature. *Aesthet Plast Surg* 2020;44:929–44.
35. Kim A, Kim SH, Kim HJ, Yang HK, et al. Ophthalmoplegia as a complication of cosmetic facial filler injection. *Acta Ophthalmol* 2016;94:e377–e379.
36. Yang HK, Lee Y, Woo SJ, Park KH, et al. Natural course of ophthalmoplegia after iatrogenic ophthalmic artery occlusion caused by cosmetic filler injections. *Plast Reconstr Surg* 2019;144:28e–34e.
37. Zhang L, Pan L, Xu H, Yan S, et al. Clinical observations and the anatomical basis of blindness after facial hyaluronic acid injection. *Aesthet Plast Surg* 2019;43:1054–60.
38. Kim YK, Jung C, Woo SJ, Park KH. Cerebral angiographic findings of cosmetic facial filler-related ophthalmic and retinal artery occlusion. *J Korean Med Sci* 2015;30:1847–55.
39. Thanasarnaksorn W, Cotofana S, Rudolph C, Kraisak P, et al. Severe vision loss caused by cosmetic filler augmentation: case series with review of cause and therapy. *J Cosmet Dermatol* 2018;17:712–8.
40. Wibowo A, Kapoor KM, Philipp-Dormston WG. Reversal of post-filler vision loss and skin ischaemia with high-dose pulsed hyaluronidase injections. *Aesthet Plast Surg* 2019;43:1337–44.
41. Chesnut C. Restoration of visual loss with retrobulbar hyaluronidase injection after hyaluronic acid filler. *Dermatol Surg* 2018;44:435–7.
42. Goodman GJ, Clague MD. A rethink on hyaluronidase injection, intraarterial injection, and blindness: is there another option for treatment of retinal artery embolism caused by intraarterial injection of hyaluronic acid? *Dermatol Surg* 2016;42:547–9.
43. Lee JI, Kang SJ, Sun H. Skin necrosis with oculomotor nerve palsy due to a hyaluronic acid filler injection [published correction appears in Arch Plast Surg. 2017 Nov;44(6):575-576]. *Arch Plast Surg* 2017;44:340–3.
44. Sharudin SN, Ismail MF, Mohamad NF, Vasudevan SK. Complete recovery of filler-induced visual loss following subcutaneous hyaluronidase injection. *Neuroophthalmology* 2018;43:102–6.
45. Surek CC, Said SA, Perry JD, Zins JE. Retrobulbar injection for hyaluronic acid gel filler-induced blindness: a review of efficacy and technique. *Aesthet Plast Surg* 2019;43:1034–40.
46. Paap MK, Milman T, Ugradar S, Goldberg R, et al. Examining the role of retrobulbar hyaluronidase in reversing filler-induced blindness: a systematic review. *Ophthalmic Plast Reconstr Surg* 2020;36:231–8.
47. Chen YC, Wu HM, Chen SJ, Lee HJ, et al. Intra-Arterial thrombolytic therapy is not a therapeutic option for filler-related central retinal artery occlusion [published correction appears in Facial Plast Surg. *Facial Plast Surg* 2018;34:325–9.
48. Peter S, Mennel S. Retinal branch artery occlusion following injection of hyaluronic acid (Restylane). *Clin Exp Ophthalmol* 2006;34:363–4.
49. Chen W, Wu L, Jian XL, Zhang B, et al. Retinal branch artery embolization following hyaluronic acid injection: a case report. *Aesthet Surg J* 2016;36:NP219–NP224.
50. Landau M. Hyaluronidase Caveats in treating filler complications. *Derm Surg* 2020;41:S347–S353.
51. Rzany B, DeLorenzi C. Understanding, avoiding, and managing severe filler complications. *Plast Reconstr Surg* 2015;136(5 suppl):196S–203S.
52. McCann M. Intravenous hyaluronidase for visual loss secondary to filler injection: a novel therapeutic approach. *J Clin Aesthet Dermatol* 2019;12:25–7.
53. Lee W, Oh W, Ko HS, Lee SY, et al. Effectiveness of retrobulbar hyaluronidase injection in an iatrogenic blindness rabbit model using hyaluronic acid filler injection [published correction appears in Plast Reconstr Surg. 2020 Jan;145(1):289]. *Plast Reconstr Surg* 2019;144:137–43.
54. Chiang C, Zhou S, Chen C, Ho DS, et al. Intravenous hyaluronidase with urokinase as treatment for rabbit retinal artery hyaluronic acid embolism. *Plast Reconstr Surg* 2016;138:1221–9.
55. Cohen JL. Understanding, avoiding, and managing dermal filler complications. *Dermatol Surg* 2008;34(suppl 1):S92–9.
56. Alam M, Tung R. Injection technique in neurotoxins and fillers: indications, products, and outcomes. *J Am Acad Dermatol* 2018;79:423–35.
57. Alam M, Tung R. Injection technique in neurotoxins and fillers: planning and basic technique. *J Am Acad Dermatol* 2018;79:407–19.
58. McGuire LK, Hale EK, Godwin LS. Post-filler vascular occlusion: a cautionary tale and emphasis for early intervention. *J Drugs Dermatol* 2013;12:1181–3.
59. Alam M, Kakar R, Nodzenski M, Ibrahim O, et al. Multicenter prospective cohort study of the incidence of adverse events associated with cosmetic dermatologic procedures: lasers, energy devices, and injectable neurotoxins and fillers. *JAMA Dermatol* 2015;151:271–7.
60. Casabona G. Blood aspiration test for cosmetic fillers to prevent accidental intravascular injection in the face. *Dermatol Surg* 2015;41:841–7.
61. DeLorenzi C. Complications of injectable fillers, part 2: vascular complications. *Aesthet Surg J* 2014;34:584–600.
62. Glaich AS, Cohen JL, Goldberg LH. Injection necrosis of the glabella: protocol for prevention and treatment after use of dermal fillers. *Dermatol Surg* 2006;32:276–81.
63. Lee W, Oh W, Oh SM, Yang EJ. Comparative effectiveness of different interventions of perivascular hyaluronidase. *Plast Reconstr Surg* 2020;145:957–64.
64. Rauso R, Zerbinati N, Franco R, Chirico F, et al. Cross-linked hyaluronic acid filler hydrolysis with hyaluronidase: different settings to reproduce different clinical scenarios. *Dermatol Ther* 2020;33:e13269.
65. Li J, Xu Y, Wang Y, Hsu Y, et al. The role of hyaluronidase for the skin necrosis caused by hyaluronic acid injection-induced embolism: a rabbit auricular model study. *Aesthet Plast Surg* 2019;43:1362–70.
66. Ciancio F, Tarico MS, Giudice G, Perrotta RE. Early hyaluronidase use in preventing skin necrosis after treatment with dermal fillers: report of two cases. *F1000Res* 2018;7:1388.
67. Fang M, Rahman E, Kapoor KM. Managing complications of submental artery involvement after hyaluronic acid filler injection in chin region. *Plast Reconstr Surg Glob Open* 2018;6:e1789.
68. Juhász ML, Marmur ES. Temporal fossa defects: techniques for injecting hyaluronic acid filler and complications after hyaluronic acid filler injection. *J Cosmet Dermatol* 2015;14:254–9.
69. Cohen JL, Biesman BS, Dayan SH, DeLorenzi C, et al. Treatment of hyaluronic acid filler-induced impending necrosis with hyaluronidase: consensus recommendations. *Aesthet Surg J* 2015;35:844–9.
70. Beleznay K, Humphrey S, Carruthers JD, Carruthers A. Vascular compromise from soft tissue augmentation: experience with 12 cases and recommendations for optimal outcomes. *J Clin Aesthet Dermatol* 2014;7:37–43.
71. Alam M, Hughart R, Geisler A, Paghdal K, et al. Effectiveness of low doses of hyaluronidase to remove hyaluronic acid filler nodules: a randomized clinical trial. *JAMA Dermatol* 2018;154:765–72.
72. Alam M, Dover JS. Management of complications and sequelae with temporary injectable fillers. *Plast Reconstr Surg* 2007;120(6 suppl):98S–105S.

73. Chauhan A, Singh S. Management of delayed skin necrosis following hyaluronic acid filler injection using pulsed hyaluronidase. *J Cutan Aesthet Surg* 2019;12:183–6.
74. Hwang CJ, Morgan PV, Pimentel A, Sayre JW, et al. Rethinking the role of nitroglycerin ointment in ischemic vascular filler complications: an animal model with ICG imaging. *Ophthalmic Plast Reconstr Surg* 2016;32:118–22.
75. Kleydman K, Cohen JL, Marmur E. Nitroglycerin: a review of its use in the treatment of vascular occlusion after soft tissue augmentation. *Dermatol Surg* 2012;38:1889–97.
76. Carley SK, Kraus CN, Cohen JL. Nitroglycerin, or not, when treating impending filler necrosis. *Dermatol Surg* 2020;46:31–40.
77. Robinson DM. In vitro analysis of the degradation of calcium hydroxylapatite dermal filler: a proof-of-concept study. *Dermatol Surg* 2018;44:S5–S9.
78. Rullan PP, Olson R, Lee KC. The use of intralesional sodium thiosulfate to dissolve facial nodules from calcium hydroxylapatite. *Dermatol Surg* 2020;46:1366–8.
79. Cassiano D, Miyuki Iida T, Lúcia Recio A, Yarak S. Delayed skin necrosis following hyaluronic acid filler injection: a case report. *Cosmet Dermatol* 2020;19:582–4.
80. Hong JY, Seok J, Ahn GR, Jang YJ, et al. Impending skin necrosis after dermal filler injection: a golden time for first-aid intervention. *Dermatol Ther* 2017;30. doi: 10.1111/dth.12440.
81. Uittenbogaard D, Lansdorp CA, Bauland CG, Boonstra O. Hyperbaric oxygen therapy for dermal ischemia after dermal filler injection with calcium hydroxylapatite: a case report. *Undersea Hyperb Med* 2019;46:207–10.
82. Zeichner JA, Cohen JL. Use of blunt tipped cannulas for soft tissue fillers. *J Drugs Dermatol* 2012;11:70–2.
83. Jones D, Bank D. Five-year postmarket safety experience with the optimal balance technology of hyaluronic acid filler. *Dermatol Surg* 2020;46:145–7.
84. Fabi SG, Champagne JP, Nettar KD, Maas CS, et al. Efficacy and safety of and patient satisfaction with injectable hyaluronic acid with 0.3% lidocaine hydrochloride for the treatment of superficial perioral lines or superficial lateral canthal lines. *Dermatol Surg* 2013;39:1613–20.
85. Beleznay K, Carruthers JD, Carruthers A, Mummert ME, et al. Delayed-onset nodules secondary to a smooth cohesive 20 mg/mL hyaluronic acid filler: cause and management. *Dermatol Surg* 2015;41:929–39.
86. Artzi O, Loizides C, Verner I, Landau M. Resistant and recurrent late reaction to hyaluronic acid-based gel. *Dermatol Surg* 2016;42:31–7.
87. Sadeghpour M, Quatrano NA, Bonati LM, Arndt KA, et al. Delayed-onset nodules to differentially crosslinked hyaluronic acids: comparative incidence and risk assessment. *Dermatol Surg* 2019;45:1085–94.
88. Beer K, Avelar R. Relationship between delayed reactions to dermal fillers and biofilms: facts and considerations. *Dermatol Surg* 2014;40:1175–9.
89. Saththianathan M, Johani K, Taylor A, Hu H, et al. The role of bacterial biofilm in adverse soft tissue filler reactions: a combined laboratory and clinical study. *Plast Reconstr Surg* 2017;139:613–21.
90. Ibrahim O, Overman J, Arndt KA, Dover J. Filler nodules: inflammatory of infectious? a review of biofilms and their implications on clinical practice. *Dermatol Surg* 2018;44:53–60.
91. Turkmani MG, De Boulle K, Philipp-Dormston WG. Delayed hypersensitivity reaction to hyaluronic acid dermal filler following influenza-like illness. *Clin Cosmet Investig Dermatol* 2019;12:277–83.
92. Humphrey S, Jones DH, Carruthers JD, Carruthers A, et al. Retrospective review of delayed adverse events secondary to treatment with a smooth, cohesive 20-mg/mL hyaluronic acid filler in 4500 patients. *J Am Acad Dermatol* 2020;83:86–95.
93. Alam M, Cohen JL, Petersen B, Schlessinger DI, et al. Association of different surgical sterile prep solutions with infection risk after cutaneous surgery of the head and neck. *JAMA Dermatol* 2017;153:830–1.
94. Dumville JC, McFarlane E, Edwards P, Lipp A, et al. Preoperative skin antiseptics for preventing surgical wound infections after clean surgery. *Cochrane Database Syst Rev* 2015;2015:CD003949.
95. Jones D, Murphy D. Volumizing hyaluronic acid filler for midface volume deficit: 2 year results from a pivotal single-blind randomized controlled study. *Dermatol Surg* 2013;39:1602–11.
96. Bitterman-Deutsch O, Kogan L, Nasser F. Delayed immune mediated adverse effects to hyaluronic Acid fillers: report of five cases and review of the literature. *Dermatol Rep* 2015;7:5851.
97. Jones D, Tezel A, Borrell M. In vitro resistance to degradation of hyaluronic acid dermal fillers by ovine testicular hyaluronidase. *Dermatol Surg* 2010;36:804–9.
98. Shumate GT, Chopra R, Jones D, Messina DJ, et al. In vivo degradation of crosslinked hyaluronic acid fillers by exogenous hyaluronidases. *Dermatol Surg* 2018;44:1075–83.
99. Gelfer A, Carruthers A, Carruthers J, Jang F, et al. The natural history of polymethylmethacrylate microspheres granulomas. *Dermatol Surg* 2007;33:614–20.
100. Jones D, Carruthers A, Brody HJ, Black JM, et al. Ten-year and beyond follow-up after treatment with highly purified liquid-injectable silicone for HIV-associated facial lipoatrophy: a report of 164 patients. *Dermatol Surg* 2019;45:941–8.
101. Lehman A, Pilcher B, Roberts WE, Schlesinger TE, et al. Postmarket experience of polymethylmethacrylate-collagen gel dermal filler. *Dermatol Surg* 2020;46:1086–91.
102. Jones DH, Carruthers A, Fitzgerald R, Sarantopoulos GP, et al. Late-appearing abscesses after injections of nonabsorbable hydrogel polymer for HIV-associated facial lipoatrophy. *Dermatol Surg* 2007;33(Suppl 2):S193–S198.
103. Daines SM, Williams EF. Complications associated with injectable soft-tissue fillers: a 5-year retrospective review. *JAMA Facial Plast Surg* 2013;15:226–31.
104. Goldan O, Georgiou I, Grabov-Nardini G, Regev E, et al. Early and late complications after a nonabsorbable hydrogel polymer injection: a series of 14 patients and novel management. *Dermatol Surg* 2007;33(Suppl 2):S199–S206.
105. Negredo E, Puig J, Ornelas A, Echeverría P, et al. Ten-year safety with polyacrylamide gel used to correct facial lipoatrophy in HIV-infected patients. *AIDS Res Hum Retroviruses* 2015;31:817–21.
106. Shen H, Lv Y, Xu JH, Hong XY, et al. Complications after polyacrylamide hydrogel injection for facial soft-tissue augmentation in China: twenty-four cases and their surgical management. *Plast Reconstr Surg* 2012;130:340e–348e.
107. Wildemore JK, Jones DH. Persistent granulomatous inflammatory response induced by injectable poly-l-lactic acid for HIV lipoatrophy. *Dermatol Surg* 2006;32:1407–9.
108. Beer K. Clinicopathologic correlation of delayed-onset periorbital poly-l-lactic acid nodules. *Dermatol Surg* 2009;35:399–402.
109. Schelke LW, Van Den Elzen HJ, Erkamp PPM, Neumann HAM. Use of ultrasound to provide overall information on facial fillers and surrounding tissue. *Dermatol Surg* 2010;36:1843–51.
110. Wortsman X. Identification and complications of cosmetic fillers. *J Ultrasound Med* 2015;34:1163–72.
111. Cassuto D, Marangoni O, De Santis G, Christensen L. Advanced laser techniques for filler-induced complications. *Dermatol Surg* 2009;35(Suppl 2):1689–95.
112. Rivers JK, Labonté-Truong N, Richer V. Adjuvant use of a 1,064 nm neodymium-doped yttrium aluminum garnet laser for the management of refractory late-onset nodules related to polymethylmethacrylate fillers [published online ahead of print]. *Dermatol Surg* 2020. doi:10.1097/DSS.0000000000002301.
113. Jones D. Treatment of delayed reactions to dermal fillers. *Dermatol Surg* 2014;40:1180.
114. Voigts R, DeVore DP, Grazer JM. Dispersion of calcium hydroxylapatite accumulations in the skin: animal studies and clinical practices. *Dermatol Surg* 2010;36:798–803.

ATTACHMENT D

Skewed Distribution of Medical Spas and Aesthetic Physician Practices: A Cross-Sectional Market Analysis

Jordan V. Wang, MD, MBE, MBA,* Christian A. Albornoz, MD,* Claire Noell, MD,† Paul M. Friedman, MD,‡ Christopher B. Zachary, MBBS, FRCP,§ and Nazanin Saedi, MD*

BACKGROUND Medical spas have experienced a recent rise in popularity by consumers. Their regulations vary from state to state, especially concerning oversight and credentialing. A majority of aesthetic physicians were shown to have a medical spa within 5 minutes of their workplace.

OBJECTIVE Our study investigated the current market distribution of medical spas and physician practices in the aesthetic field.

MATERIALS AND METHODS For the 30 most populous cities, data were collected for medical spas and aesthetic physicians. Descriptive ratios were calculated, and various local factors were examined.

RESULTS The cities with the greatest number of medical spas were New York (374), Houston (297), and Los Angeles (227). The cities with the greatest number of aesthetic physicians were New York (365), Houston (135), and Chicago (122). Population size had significant relationships with number of medical spas ($p < .000001$) and aesthetic physicians ($p < .000001$). For ratio of medical spas to aesthetic physicians, the top cities were Las Vegas (9.17), Denver (3.86), and San Jose (3.65). In total, 73.3% of cities had more medical spas than aesthetic physicians.

CONCLUSION Certain cities have experienced an unequal distribution of medical spas. Further research should examine how this affects consumer decision-making for the selection of practice settings.

The authors have indicated no significant interest with commercial supporters.

Medical spas are cosmetic facilities that can offer many minimally invasive and energy-based treatments that were once traditionally performed at physician-based practices. These aesthetic procedures are now offered in a commercial setting, frequently at greatly discounted prices and with shorter wait times, both of which have been shown to play a role in aesthetic consumer decision-making processes.[1] In 2018, a consumer survey by the American Society for Dermatologic Surgery (ASDS) revealed that 70% of respondents were actively considering a cosmetic procedure.[2] Because of our culture's growing interest in aesthetic appearance and the expanding mainstream acceptance of cosmetic interventions, the popularity of medical spas has surged in recent years. With such prominent consumer demand, it comes as no surprise that in 2018, there were about 5,400 medical spas across the country with an estimated net worth approaching $10 billion.[3] This complements a recent study demonstrating that most aesthetic physicians had a medical spa within 5 minutes of their workplace.[4]

As medical spas continue to proliferate, there has been a lack of standardized regulations, which has resulted in strikingly disparate regulatory practices

Department of Dermatology and Cutaneous Biology, Thomas Jefferson University, Philadelphia, Pennsylvania; †Maryland Dermatology Laser, Skin, and Vein Institute, Hunt Valley, Maryland; ‡Dermatology and Laser Surgery Center, Houston, Texas; §Department of Dermatology, University of California, Irvine, California

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.dermatologicsurgery.org).

ISSN: 1076-0512 • Dermatol Surg 2020;00:1–4 • DOI: 10.1097/DSS.0000000000002687

across state lines. The absence of uniform rules and regulations has led to wildly varying degrees of oversight and credentialing processes for these facilities. It is likely that this has contributed to their high degree of aesthetic complications.[4] In addition, government efforts to increase access to primary health care through reduced regulation of physician extenders have inadvertently accelerated the influx of non-physician providers into the more financially lucrative medical spa setting. All of this has occurred despite vocal opposition from numerous medical societies, such as the ASDS and American Academy of Dermatology.[5,6]

In a rapidly changing field, it may benefit practitioners to better understand the market in which they practice, in hopes that they can accurately gauge where they currently stand, develop strategies for improvements in marketing and gains in efficiency, and forecast the anticipated changes to come. Our study offers a current cross-sectional analysis of the cosmetic market for medical spas and aesthetic physician practices in the most populous cities in the United States. By studying the distribution and relative ratios of medical spas and aesthetic physicians, especially in relation to local and regional factors, we aim to provide a more complete picture of the current aesthetic landscape in the United States.

Materials and Methods

The 30 most populous cities were determined using data provided by the United States Census Bureau. Data were collected in November 2019 for medical spas from the Yelp database, dermatologic surgeons from the ASDS, and plastic surgeons from the American Society of Plastic Surgeons (ASPS) in these 30 cities. These databases were selected because they were comprehensive, updated, accurate, readily available, and relatively straightforward for gathering the desired information. There was no verified and comprehensive database to gather information for medical spas. The ASDS and ASPS databases allowed screening for only registered and verified practitioners. However, it is important to note that not all dermatologic surgeons and plastic surgeons are registered members of these societies. Data were filtered for addresses that included only the respective city in an attempt to standardize collection methods between cities, which may differ in zoning and city limit demarcation. Data for median household income for counties were provided by the United States Census Bureau from their American Community Survey 5-year estimates 2013 to 2017. Descriptive ratios were calculated, including numbers per 10,000 persons of the city's total population, and various local factors were examined.

Results

The top 5 cities by population were New York, Los Angeles, Chicago, Houston, and Phoenix. The 5 cities with the greatest number of medical spas were New York (374), Houston (297), Los Angeles (227), Las Vegas (211), and Chicago (166). The 5 cities with the greatest number of aesthetic physicians were New York (365), Houston (135), Chicago (122), Dallas (106), and San Antonio (79). Population size had significant relationships with the number of medical spas ($p < .000001$) and aesthetic physicians ($p < .000001$).

For number of medical spas per 10,000 persons, the top 5 cities were Las Vegas (3.27), Denver (1.56), Austin (1.48), Houston (1.28), and San Diego (1.09) (See **Supplemental Digital Content 1**, Table S1, http://links.lww.com/DSS/A464). For number of aesthetic physicians per 10,000 persons, the top 5 cities were Boston (1.02), San Francisco (0.83), Dallas (0.79), Washington D.C. (0.71), and Austin (0.69) (See **Supplemental Digital Content 2**, Table S2, http://links.lww.com/DSS/A465). For ratio of medical spas to aesthetic physicians, the top 5 cities were Las Vegas (9.17), Denver (3.86), San Jose (3.65), Los Angeles (3.39), and Phoenix (2.48) (See **Supplemental Digital Content 3**, Table S3, http://links.lww.com/DSS/A466). The mean ratio of medical spas to aesthetic physicians was 1.82. In total, 73.3% of cities had more medical spas than aesthetic physicians.

When comparing by region, cities in the West had the greatest mean number of medical spas per 10,000 persons (1.17), followed by the South (0.73), the Northeast (0.45), and the Midwest (0.33). For aesthetic physicians, the Northeast had the greatest mean

number per 10,000 persons (0.62), followed by the South (0.52), the West (0.44), and the Midwest (0.38). The median household income had no significant relationship with either number of medical spas (p = .4498) or aesthetic physicians (p = .3210).

Discussion

The aesthetic market for minimally invasive and energy-based treatments has continued to expand over the past several years and shows no current signs of slowing. The annual revenue generated by cosmetic medicine has been estimated to be several billions of dollars.[7] Numerous factors, such as advances in medical technologies, competitive and targeted pricing strategies, broadening mainstream acceptance of cosmetic interventions, and minimal wait times, have all likely contributed to the rise of the aesthetic industry. Unsurprisingly, the highest concentrations of medical spas and aesthetic physicians occur in the largest metropolitan areas, where aggressive marketing campaigns often produce the highest yields. It is also important to note that those behind medical spas often possess a business background, whereas dermatologists are generally not exposed to a comprehensive education covering business skills during their training.[8] Our study supports that local population size may have an effect on the numbers of medical spas and aesthetic physicians that are available to patients.

Of the 5 most populous cities in the United States, only Houston remained in the top 5 for the ratio of medical spas per 10,000 persons. By contrast, Las Vegas, the 28th most populous city in the United States, had by far the greatest ratio of medical spas relative to not just the population but also to the number of aesthetic physicians. Las Vegas' medical spa to aesthetic physician ratio was nearly 3 times greater than the next highest city. We surmise that the reason as to why Las Vegas provides a more fertile ground for these cosmetic facilities is due to its booming tourism industry, which brought in more than 42 million visitors in 2018 alone.[9] Such a tourist-heavy destination may be considered ideal for medical spas, where thousands of daily visitors can be drawn in by affordable aesthetic procedures that offer little to no downtime in a convenient—if not luxurious—setting.

However, Las Vegas is clearly an outlier city, and tourism alone does not account for why all states or geographic regions are overrepresented in this study. As demonstrated, local population and regional factors may also be predictors of the relative density of medical spas and aesthetic physicians. San Antonio and Dallas, the seventh and ninth most populous cities, respectively, joined Houston in granting Texas the distinction of having 3 of the top 5 cities in the country for total number of aesthetic physicians. Austin and Houston also had the third and fourth highest ratios, respectively, of medical spas per 10,000 persons, cementing Texas' position as a cosmetic hotbed. Part of the popularity of aesthetic procedures in Texas may be sociocultural, and treatments may be more accepted there compared to other locations. Further research should look into local factors that may be contributing to these trends.

Certainly, other variables may play a role in affecting the distribution in the cosmetic market. States with more lax regulations on supervision and delegation may be viewed by business owners as more attractive destinations to open medical spas compared to stricter states. For example, Texas, New York, and Maryland represent a few of the states that allow for physician discretion in the delegation of minimally invasive cosmetic procedures at medical spas to nonphysicians.[10] Such vague regulatory statutes were highlighted in a recent study that shed light on the wide range of regulations governing medical spas and how they differ from state to state.[11]

The lack of a uniform regulatory framework demands further analysis of how state-specific regulations affect both the prevalence of medical spas and their associated patient complications. With the growing number of nonphysicians offering aesthetic procedures at these facilities, there may be particular states where medical spas are putting patients at a greater risk. Studies have already shown that dermatologists and nondermatologists alike are increasingly delegating procedures to nonphysicians.[12,13] In total, 73.3% of the cities in our study had more medical spas than aesthetic physicians, raising potential concerns for patient safety across the country. Some states may even allow naturopaths to serve as a medical director for medical spas.[14]

ATTACHMENT D

Unfortunately, not all state medical boards have statutes requiring mandatory reporting of adverse events.[10] In this instance, data from the medicolegal literature may offer a proxy for the number of aesthetic complications. From 2008 to 2011, the percentage of medical professional liability claims stemming from cutaneous laser surgery performed by nonphysicians increased by nearly 115%, with procedures performed by nonphysicians in medical spas accounting for nearly 80% of the lawsuits.[15] To protect our patients, more efforts should be focused on reforming current legislation as the ASDS Association (ASDSA) has attempted to accomplish with its proposed "Medical Spa Safety Act," which would ensure safer practice guidelines for medical spas.[16]

Although limited by the number of cities examined and lack of available, verified, and comprehensive databases from which to gather data, our study attempted to shed light on the distribution of medical spas and aesthetic physicians in the most populous cities in the United States, while also examining local factors that may play a role. Our data, particularly the ratio of medical spas to aesthetic physicians, begin to offer insights into local variations, but further research is still needed to investigate how state regulations affect the prevalence of medical spas. Furthermore, these data may aid future studies comparing medical spas with aesthetic physicians, especially in regard to local incidence of associated patient complications. The goals of any current and upcoming research should be to improve the safety of our patients and raise awareness of any discrepancies between medical spas and physician-based practices.

Conclusion

In the United States, certain cities have experienced an unequal distribution of medical spas. Many cities have more medical spas than aesthetic physicians, and local factors, such as population size and state regulations of medical spas, may play a role. The distribution of available cosmetic facilities can affect consumer decision-making for the practice setting that they select, which could in turn impact patient care. Additional research is needed to examine differences in patient safety and outcomes between medical spas and physician practices for various localities.

References

1. Wang JV, Zachary CB, Saedi N. Factors influencing consumer decisions in aesthetics: selection of procedures and practitioners. Dermatol Surg 2020. Epub Ahead of Print.
2. American Society for Dermatologic Surgery. *ASDS Consumer Survey on Cosmetic Dermatologic Procedures*; 2018. Available from: https://www.asds.net/medical-professionals/practice-resources/asds-consumer-survey-on-cosmetic-dermatologic-procedures. Accessed January 22, 2020.
3. American Med Spa Association. *Medical Spa State of the Industry: Executive Summary*; 2019. Available from: https://www.americanmedspa.org/page/med-spa-statistics. Accessed January 22, 2020.
4. Wang JV, Albornoz CA, Goldbach H, Mesinkovska N, et al. Experiences with medical spas and associated complications: a survey of aesthetic practitioners. Dermatol Surg 2020. Epub Ahead of Print.
5. American Society for Dermatologic Surgery Association. *Position on Physician Oversight of Medical Spas*. Available from: https://www.asds.net/Portals/0/PDF/asdsa/asdsa-position-statement-physician-oversight-in-medical-spas.pdf. Accessed January 22, 2020.
6. American Academy of Dermatology Association. *Position Statement on Medical Spa Standards of Practice*. Available from: https://www.aad.org/forms/policies/uploads/ps/ps-medical%20spa%20standards%20of%20practice.pdf. Accessed January 22, 2020.
7. Ahn CS, Davis SA, Dabade TS, Williford PM, et al. Cosmetic procedures performed in the United States: a 16-year analysis. Dermatol Surg 2013;39:1351–9.
8. Wang JV, Albornoz CA, Hazan E, Keller M, et al. Business administration training for dermatology residents: preparing for the business of medicine. Clin Dermatol 2019;37:78–9.
9. Las Vegas Statistics. *The Ultimate List of Statistics on Las Vegas for*; 2019. Available from: https://lasvegasstatistics.com. Accessed February 1, 2020.
10. Choudhry S, Kim NA, Gillum J, Ambavaram S, et al. State medical board regulation of minimally invasive cosmetic procedures. J Am Acad Dermatol 2012;66:86–91.
11. DiGiorgio CM, Avram MM. Laws and regulations of laser operation in the United States. Lasers Surg Med 2018;50:272–9.
12. Austin MB, Srivastava D, Bernstein IH, Dover JS. A survey comparing delegation of cosmetic procedures between dermatologists and nondermatologists. Dermatol Surg 2015;41:827–32.
13. Brody HJ, Geronemus RG, Farris PK. Beauty versus medicine: the nonphysician practice of dermatologic surgery. Dermatol Surg 2003; 29:319–24.
14. Gibson JF, Srivastava D, Nijhawan RI. Medical oversight and scope of practice of medical spas (med-spas). Dermatol Surg 2019;45:581–7.
15. Jalian HR, Jalian CA, Avram MM. Increased risk of litigation associated with laser surgery by nonphysician operators. JAMA Dermatol 2014;150:407–11.
16. American Society for Dermatologic Surgery Association. *Model Legislation of Medical Spa Safety Act*. Available from: https://www.asds.net/Portals/0/PDF/asdsa/asdsa-medical-spa-safety-act.pdf. Accessed January 25, 2020.

Address correspondence and reprint requests to: Jordan V. Wang, MD, MBE, MBA, Department of Dermatology and Cutaneous Biology, Thomas Jefferson University, 833 Chestnut Street, Suite 740, Philadelphia, PA 19107, or e-mail: drjordanwang@gmail.com

Original Article

Supervision Unveiled: Navigating the Supervision Landscape in Medical Spas

Rawaa M. Almukhtar, MD, MPH,* Alyx Rosen Aigen, MD,† Jameson Loyal, MD,‡ and Vineet Mishra, MD§

BACKGROUND There is an ongoing increase in the demand for injectable procedures and an increase in the number of medical spas across the United States State regulations significantly vary regarding level of supervision at these medical spas.

OBJECTIVE The aim of this study was to determine who performs cosmetic procedures, provides medical supervision, and who is being informed of complications.

METHODS Descriptive study based on a standardized telephone interview performed by a prospective patient for injectable treatments performed at medical Spas in Las Vegas. Data were then extracted and analyzed.

RESULTS Of 63 medical spas reviewed, most of the injectable treatments (73%) were performed by nonphysicians. An onsite physician who supervised or personally performed the cosmetic procedures was present in only 38.1% of the spas surveyed. Only 46% of surveyed medical spas notify a medical director/supervising physician in the event of a complication and only 39.7% of surveyed spas had a number to call after regular business hours.

CONCLUSION The majority of treatments are performed by nonphysicians in the spas surveyed. Physician supervisors are not on site in most of the spas and about half of spas do not inform the medical director in the event of a complication.

There is an ongoing increase in the demand for minimally invasive cosmetic procedures. The 2023 American Society for Dermatologic Surgery (ASDS) Survey on Dermatologic Procedures showed that 70% of consumers are interested in a cosmetic procedure.[1] According to the 2018 ASDS Survey on Dermatologic Procedures, over 3.7 million injectable procedures were performed.[2] Injection of filler products experienced a 78% increase from 2012.[2] Laser, light, and energy-based treatments grew by 74%, and body sculpting procedures increased over 400% during this time period.[2] The increasing popularity of aesthetic treatments has contributed to the trend of medical spas opening across the country. In 2022, there are 8,841 medical spas, up from 7,430 in 2021 and 5,431 in 2018. The average annual medical spa revenue in 2022 is $1,982,896 up from $1,526,382 in 2018.[3]

The efforts of states to improve access to health care by loosening the regulations for nonphysician providers has contributed to the lack of strict regulations regarding physician supervision at medical spas.[4] State regulations significantly vary regarding level of supervision at these medical spas and type of accreditation needed to perform these procedures.[5] A recent study demonstrated that the majority of medical directors were not trained in either dermatology or plastic surgery. Additionally, nearly 30% of medical spas in the study had a medical director who did not perform any procedures themselves, and nearly half were off-site the majority of the time.[6]

The aim of this study was to determine who performs cosmetic procedures, who provides medical supervision, and who is being informed of complications which might take place after injectable procedures are performed at medical spas. A recent study showed Las Vegas had one of the highest ratios of medical spas to aesthetic physicians (dermatologic surgeons and plastic surgeons) in the country, thus, we decided to perform the survey of medical spas in Las Vegas.[7]

Methods

The authors queried Google, Facebook, and Yelp websites with the search terms "medical spa," "medi-spa," "med-spa," and "Las Vegas." The queries yielded 114 medical spas in the Las Vegas area. Websites were reviewed, and contact information, available services, and medical director information, if available, were recorded. Of the 114 medical spas found, 73 met the inclusion criteria based on working number, active providers performing procedures, and procedures of interest being performed. A script regarding inquiry for new patient services was developed by the authors. A prospective patient then contacted the 73 medical spas through telephone between July and

*From the *Department of Dermatology, Scripps Medical Group, San Diego, California; †Dr. Philip Frost Department of Dermatology and Cutaneous Surgery, University of Miami, Miami, Florida; ‡West Dermatology, San Diego, California; §Department of Dermatology, University of California San Diego (UCSD), San Diego, California*

This study was funded by The American Society for Dermatologic Surgery.

The authors have indicated no significant interest with commercial supporters.

R. M. Almukhtar and A. R. Aigen are co-first authors.

Address correspondence and reprint requests to: Rawaa Almukhtar, MD, MPH, Scripps Medical Group, 9898 Genesee Ave, La Jolla 92037, CA, or e-mail: rawa.almukhtar@gmail.com

Dermatol Surg 2024;50:954–957
http://dx.doi.org/10.1097/DSS.0000000000004248

September of 2023 and recorded responses from staff. Information was collected, extracted into a useable data set, and analyzed using R . This study did not involve experimentation on human subjects and is exempt from Institutional Review Board review. The authors were responsible for the database queries, review, and analysis.

Results

Seventy-three medical spas were contacted. 63 medical spas at which injectable treatments were performed were included in the analysis. The most common injectable treatments performed at the spas were neuromodulator injections (83.6%), followed by soft-tissue dermal filler injections (78.1%), and deoxycholic acid (65.8%).

Nonphysicians performed the injectable treatments at most of the medical spas in this study (73%; Figure 1). A supervising physician was available to conduct an in-person cosmetic consultation at only 25.4% of surveyed medical spas. An onsite physician supervises or personally performs cosmetic procedures on-site at less than half (38.1%) of the medical spas queried (Figure 2).

Among those supervising physicians, only 21.4% were board certified in dermatology or plastic surgery. The top identified medical specialties of medical spa directors were internal medicine and family medicine (Table 1). In the event of a complication or unwanted side effect from a cosmetic procedure, only 46% of surveyed medical spas notify a medical director/supervising physician. 39.7% of surveyed spas had no number to call after regular business hours. When looking at available website and social media accounts for the medical spas, it is unclear who is performing the treatment in 62.5% of the spas.

Discussion

Our study found that most of the injectable treatments (73%) were performed by nonphysicians and an onsite physician who supervised or personally performed the cosmetic procedures was present in only 38.1% of the spas surveyed. Furthermore, the physician supervisors' board certification was not in dermatology or plastic surgery in most of the spas surveyed (78.6%). Such lack of proper physician supervision is not unique to 1 geographical area. A recent study by Hogan and colleagues found a similar pattern where 127 medical spas in the Chicago area were surveyed.[8] A supervising physician was not on-site at 81.1% of the facilities. Patients were informed of the lack of supervising physician at 64.6% of the surveyed medical spas.

Over the past decade, the surge in demand for cosmetic procedures has led to a proliferation of medical spas in the United States.[9] A survey by the American Society of Plastic surgery in 2022 showed a 73% and 70% increase in neurotoxin and hyaluronic acid filler injections, respectively, compared with pracademic volume.[10] Guidelines regarding the definition of a medical procedure, the delegation of such procedures, on-site versus off-site physician supervision, and the type of certification required by staff performing the procedure are determined by state

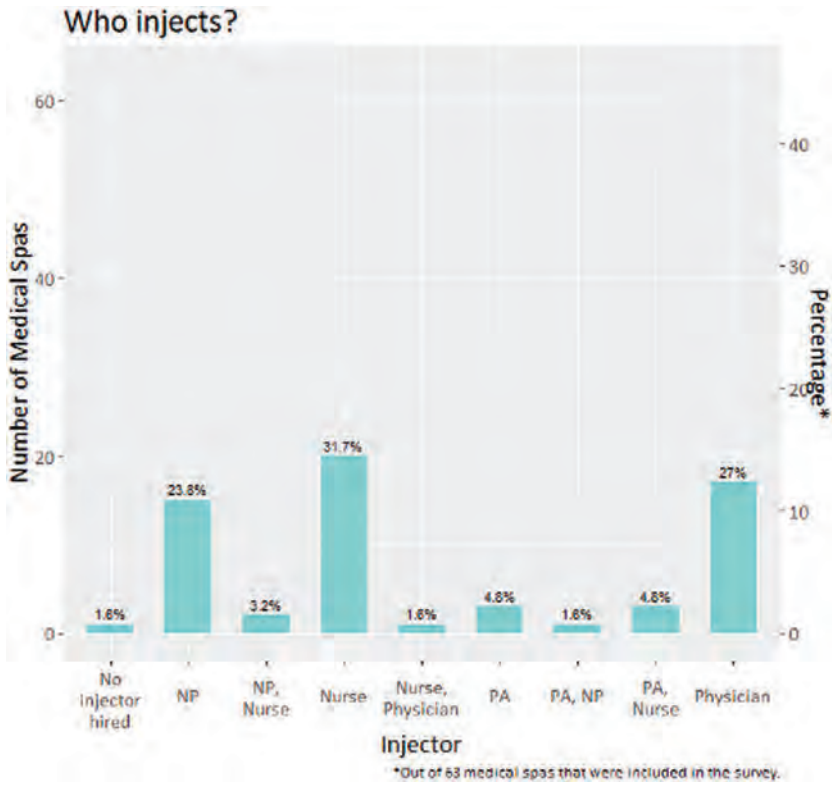


Figure 1. Medical spa cosmetic procedure provider by training.

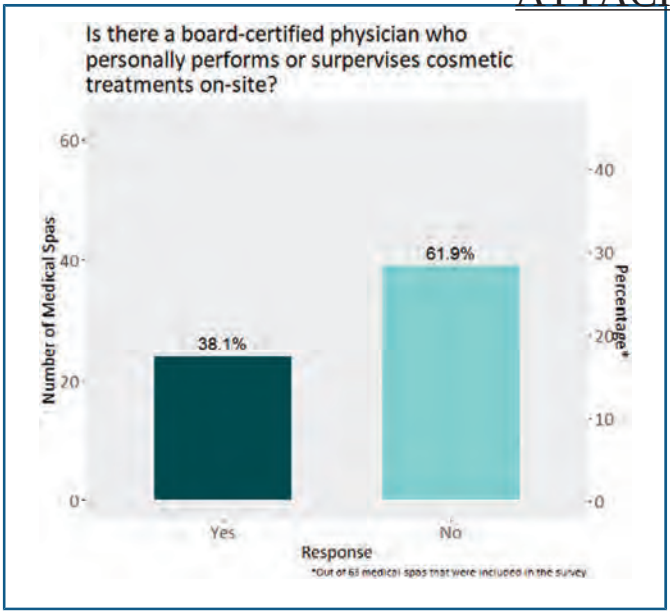


Figure 2. Board-certified physicians performing cosmetic treatments at study medical spas.

medical boards and vary widely from 1 state to another.[4,6] In most states, nonphysician practitioners are required to work under the supervision of a licensed physician, who is responsible for overseeing patient care. However, in many cases, these supervising physicians do not need to be on-site but rather be available to be reached when necessary.[6] While the board requires that medical spas have a designated medical director who is a licensed physician, the board does not require the supervising physician to be present on site. Under Nevada State Statue NRS 454 and 629.086, the state only allows neurotoxin and filler injections to be performed by licensed physicians, physician assistants, properly trained dentists, registered nurses (RN), advanced practice nurse practitioners (ARNP), and podiatric physicians. A study by Gibson and colleagues surveyed med-spas in the most heavily populated cities and showed that 72% of the spas advertised a medical director on their website.[6] Of the listed medical directors, 41% were trained in dermatology and/or plastic surgery. In phone interviews, 52% stated that the medical director was on site less than 50% of the time.[6]

TABLE 1. Study Medical Spa Directors or Supervising Physicians by Medical Specialty

What is the Physician Board-Certified in?	Frequency
Anesthesiology	1
Dermatology	1
Family medicine	9
General surgery	1
Internal medicine	10
Pain management	1
Plastic surgery	5

Legend.

In a study by Rossi and colleagues,[11] consumers of cosmetic procedures and physician members of the American Society for Dermatologic Surgery (ASDS) were surveyed. Patients treated by nonphysicians experienced more complications compared to physicians. Another survey of ASDS members showed that, of all cosmetic complications encountered by surveyed members in the previous 2 years, 61% to 100% were attributable to medical spas.[12] The most commonly cited complications from medical spas were laser burns, discoloration following laser treatment, and filler misplacement, whereas the most commonly cited treatments resulting in complications were injectable fillers, intense pulsed light, and laser hair removal. In addition, there has been increased risk of complications and litigation of cosmetic procedures performed by nonphysicians outside a traditional medical setting.[13–15]

Of note, our study showed that in the event of a complication or unwanted side effect from a cosmetic procedure, only 46% of surveyed medical spas notify a medical director/supervising physician and only 39.7% of surveyed spas had number to call after regular business hours. These results highlight the concern about management of complications that might occur following a procedure performed at those spas.

The surveyed members emphasize the vital role of a physician's comprehensive training in anatomy and injectable procedures in preventing and managing complications associated with these treatments.

Possible limitations of the study include that with the geography of the study being limited to Las Vegas, nationwide conclusions are difficult to determine. Further studies are needed to better understand medical spa practice across the country.

Conclusion

There is significant variation in the supervision of injectable procedures performed in the medical spas surveyed with the majority of treatments performed by nonphysicians. Physician supervisors or medical directors were not on site in most of the spas, and less than half of them were informed in the event of a complication or unwanted side effect from an injectable procedure. Improved regulations of cosmetic procedures performed at medical spas, guidelines regarding on-site versus off-site supervision, and staff accreditation and training are needed to protect patient safety.

References

1. Surgery. *ASfD. 2023 ASDS Survey on Dermatologic Procedures*. Available from: https://www.asds.net/medical-professionals/practice-resources/consumer-survey-on-cosmetic-dermatologic-procedures. Accessed December 25, 2023.
2. American Society for Dermatologic Surgery. *2018 ASDS Survey on Dermatologic Procedures*. Available from: https://www.asds.net/portals/0/PDF/procedures-survey-results-infographic-2018.pdf. Accessed December 25, 2023.
3. *The 2022 Medical Spa State of the Industry Executive Summary*. Available from: https://americanmedspa.org/. Accessed December 25 2023.

4. Wang JV, Shah S, Albornoz CA, Rohrer T, et al. Medical spa or physician practice: the national impact of patient wait times in aesthetics. *Dermatol Surg* 2021;47:887–9.
5. Choudhry S, Kim NA, Gillum J, Ambavaram S, et al. State medical board regulation of minimally invasive cosmetic procedures. *J Am Acad Dermatol* 2012;66:86–91.
6. Gibson JF, Srivastava D, Nijhawan RI. Medical oversight and scope of practice of medical spas (med-spas). *Dermatol Surg* 2019;45:581–7.
7. Wang JV, Murgia RD, Noell C, Saedi N, et al. National market analysis for body contouring providers: medical spas and physician practices. *J Cosmet Dermatol* 2021;20:1663–7.
8. Hogan S, Wood E, Mishra V. Who is holding the syringe? A survey of truth in advertising among medical spas. *Dermatol Surg* 2023;49:1001–5.
9. Valiga A, Albornoz CA, Chitsazzadeh V, Wang JV, et al. Medical spa facilities and nonphysician operators in aesthetics. *Clin Dermatol* 2022;40:239–43.
10. *2022 ASPS Procedural Statistics Release*. Available from: https://www.plasticsurgery.org/documents/News/Statistics/2022/plastic-surgery-statistics-report-2022.pdf. Accessed Dec 25 2023.
11. Rossi AM, Wilson B, Hibler BP, Drake LA. Nonphysician practice of cosmetic dermatology: a patient and physician perspective of outcomes and adverse events. *Dermatol Surg* 2019;45:588–97.
12. Wang JV, Albornoz CA, Goldbach H, Mesinkovska N, et al. Experiences with medical spas and associated complications: a survey of aesthetic practitioners. *Dermatol Surg* 2020;46:1543–8.
13. Jalian HR, Jalian CA, Avram MM. Increased risk of litigation associated with laser surgery by nonphysician operators. *JAMA Dermatol* 2014;150:407–11.
14. Jalian HR, Jalian CA, Avram MM. Common causes of injury and legal action in laser surgery. *JAMA Dermatol* 2013;149:188–93.
15. Woodward J, Khan T, Martin J. Facial filler complications. *Facial Plast Surg Clin* 2015;23:447–58.

Original Article

The Differences in the Practice of Cosmetic Dermatologic Procedures Between Physicians and Nonphysicians

Abdullah Aleisa, MD,* Jasmine Thai Lu, BS,† Aljohara Al Saud, MD,‡ Inge J. Veldhuizen, MD, PhD,§ Anthony M. Rossi, MD,‖ and Kachiu C. Lee, MD MPH¶

BACKGROUND With a rise in demand for cosmetic dermatologic procedures comes an increase in nonphysician providers performing such procedures. However, little is known about the practice of cosmetic procedures performed by nonphysicians.

OBJECTIVE To assess the differences in the practice of cosmetic procedures provided by physicians and nonphysicians.

MATERIALS AND METHODS A cross-sectional analysis was performed using participant ($n = 4,062$) responses to an 18-point, web-based survey about previous cosmetic procedures.

RESULTS In total, 1,328 participants reported having previous cosmetic procedures done by a physician ($n = 828$), a nonphysician ($n = 413$), or an unknown provider ($n = 87$). Respondents of all age ranges and male respondents ($p < .001$) tended to choose physicians over nonphysician providers when choosing a practice. Moderate adverse events were more frequently seen when nonphysician providers completed cosmetic procedures ($p < .001$). Despite a higher frequency (73.3% vs 51.8%) of more moderate complications seen in procedures done by nonphysician providers, over 70% of respondents believe that nonphysician providers are qualified enough to continue performing cosmetic procedures.

CONCLUSION People should be encouraged to make an informed decision when choosing a provider because cosmetic procedures are still considered medical procedures.

Cosmetic dermatologic procedures, such as neurotoxins, fillers, laser hair removal, or chemical peels, have become increasingly popular in the United States during recent years. According to the American Society for Dermatologic Surgery (ASDS), there was an increase in the number of cosmetic procedures completed in the United States, rising from 12.5 million procedures in 2018 to 14 million procedures in 2019.[1,2] With an increasing demand for cosmetic dermatologic procedures, there is an accompanying rise of nonphysician providers performing cosmetic procedures in nonmedical settings. As delegated by 48% of state boards, unlicensed nonphysician providers are permitted to perform cosmetic procedures under the assumption that there has been adequate training.[3] However, in a 2014 survey conducted by Rossi and colleagues,[4] there was a higher number of skin discoloration and burns when cosmetic procedures were performed by nonphysicians in a spa setting, with improper technique by nonphysician providers being the most common cause.

A different study done in millennials, defined as those born between 1981 and 1996, found that 70% of surveyed patients thought that physician practices were"more trustworthy" in comparison with medical spas.[3] In total, 72% of the surveyed patients reported interest in returning for future procedures done at a physician practice, but only 56% of patients indicated that they were interested in returning to a medical spa, with credentials, safety, and reputation cited as the most highly valued parameters for selecting or reselecting a practice.[3] Although research has established that patients tend to prefer physician practices to medical spas likely because of implied greater safety, there is little literature that explores patient-reported complications of procedures done by physicians compared with nonphysicians.

Although increasingly common to have cosmetic procedures done by nonphysician providers, patient safety in such situations continue to be a concern. The purpose of this study was to compare patient-reported differences in the practice of cosmetic procedures performed by physicians and nonphysicians.

Methods

An 18-point, web-based targeted survey pertaining to previous cosmetic procedures was delivered through

*From the *Department of Dermatology, King Saud University, Riyadh, Saudi Arabia; †Drexel University College of Medicine, University of California, Irvine; ‡College of Medicine, AlFaisal University, Riyadh, Saudi Arabia; §Department of Plastic and Reconstructive Surgery, Catharina Hospital, Eindhoven, the Netherlands; ‖Dermatology Division, Memorial Sloan Kettering Cancer Center, New York, New York; ¶Main Line Center for Laser Surgery, Ardmore, Pennsylvania*

Supported by the American Society for Dermatologic Surgery—Future Leaders Network.

The authors have indicated no significant interest with commercial supporters.

A. Aleisa and J. T. Lu contributed equally to this work.

Address correspondence and reprint requests to: Abdullah Aleisa, MD, King Saud University, Riyadh, Saudi Arabia, or e-mail: abdullah213@gmail.com

Dermatol Surg 2023;49:1165–1169
http://dx.doi.org/10.1097/DSS.0000000000003948

electronic mail to respondents 18 years of age and above, in all regions of the United States using Survey Monkey (http://www.SurveyMonkey.com). Respondents answered by completing and returning the survey electronically via the web.

The survey contained multiple-choice questions regarding the type of provider, the location where the procedure was performed in, adverse events, influential factors in choosing a provider, and perceptions regarding type of provider.

A cross-sectional analysis was performed using participant (n = 4,062) responses to the web-based survey. Written informed consent was obtained for each participant. Responses were analyzed using Chi-square test for categorical variables and the t-test for continuous variables, with $p < .05$ considered statistically significant.

Results

Of the 4,026 survey participants, 1,328 participants (33%) reported that they had previous cosmetic procedures done by a physician (n = 828, 62%), a nonphysician (n = 413, 31%), or an unknown provider (n = 87, 7%). Physician providers were most commonly dermatologists, plastic surgeons, and facial plastic surgeons, whereas nonphysician providers were most commonly estheticians/cosmetologists, physician assistants, nurses, medical assistants, and medical spa employees. Of the providers performing procedures, dermatologists comprised 48% of physicians and estheticians/cosmetologists comprised 42% of nonphysicians.

Respondents Demographics

Respondents within ages 25 to 34 years were more likely to have cosmetic procedures (p = .002). The most common respondents to the survey were respondents residing in Southern US regions and reporting an annual household income of $50,000–74,999. Respondents in all groups tended to select physician providers more often than nonphysician providers for procedures (Table 1). Male respondents were significantly more likely to have their cosmetic procedures done by physicians, whereas female respondents were more likely to have procedures done by nonphysician providers ($p < .001$).

Cosmetic Procedure Providers

In all surveyed procedure types, physicians were more often the performing provider, with laser hair removal treatments as the least frequent procedures done by physicians (55% of all providers), but the most frequent procedures done by nonphysician providers (37% of all providers). Moreover, hair transplantation was done by mostly physicians (79% of all providers). Laser and light treatments, chemical peels, laser hair removal treatments, and microdermabrasions were outsourced to nonphysician providers approximately one-third of the time (Figure 1).

There was a significant difference in severity of adverse events when cosmetic procedures were performed by physicians compared with nonphysician providers ($p < .001$). Respondents reported having more moderate adverse events when having cosmetic procedures done by a nonphysician provider (n = 55, 73.3%), whereas respondents reported having more mild than moderate or severe adverse events when procedures were done by a physician provider (n = 125, 41.8%). There was no statistically significant difference in adverse events between different physician specialties.

Influential Factors in Choosing a Provider

The most influential factor for choosing any provider (physician and nonphysician) was a referral from a physician. Most respondents who ultimately chose a nonphysician over a physician cited price as the reason (Table 2).

Perceptions Regarding the Type of Provider

In total, 70.3% of the respondents (n = 394) believed that nonphysicians were qualified to perform cosmetic procedures. The most commonly cited reason for belief that nonphysician providers were not qualified being "inadequate level of training" (n = 295, 74.9%). Patient suggestions to limit frequency of adverse events included having a physician in the room or on-site during procedures, more thorough training or certification processes, and restricting the scope of practice for nonphysician providers to only performing less invasive cosmetic procedures.

Discussion

Although approximately one-third of cosmetic procedures done are performed by nonphysician providers, the survey results demonstrate that adverse events after procedures completed by nonphysician providers are more likely to be greater in severity than complications after procedures completed by physician providers. Furthermore, many cosmetic procedures are being performed by estheticians/cosmetologists. Men were more likely to choose physicians over nonphysicians for their cosmetic treatments. There were no significant differences in the practice of cosmetic procedures performed by the different specialties of physicians.

A potential explanation could be the robust surgical training and anatomy education through exposure to cadavers in medical schools that build the foundation of cosmetic procedures. Further, longer educational and training requirements mandated of physicians in comparison with nonphysician providers. After obtaining a baccalaureate/bachelor's degree from an accredited university, physicians are required to undergo a minimum 7 years of medical training, pass an end-of-residency examination to become officially board certified for independent practice, and fulfill Maintenance of Certification requirements by passing a recertification examination every 10 years.[5] In contrast, in Pennsylvania, estheticians are

TABLE 1. Demographics of Respondents Who had Cosmetic Procedures

% of Provider Type	Physicians	Nonphysicians	Unknown	*p*
Age (yr)				.002
25–34 (*n* = 342)	65.79	25.15	9.06	
35–44 (*n* = 419)	66.35	27.45	6.21	
45–54 (*n* = 349)	59.03	35.53	5.44	
>55 (*n* = 217)	54.38	40.55	5.07	
Gender				<.001
Male (*n* = 540)	73.33	19.81	6.85	
Female (*n* = 774)	54.91	38.76	6.33	
Region of residence in the United States				.114
Northeast (*n* = 290)	66.90	26.90	6.21	
Midwest (*n* = 215)	56.28	37.21	6.51	
South (*n* = 439)	62.41	31.21	6.38	
West (*n* = 371)	63.34	29.65	7.01	
Household income ($)				.162
50,000–74,999 (*n* = 444)	63.51	28.15	8.33	
75,000–99,999 (*n* = 318)	60.38	32.70	6.92	
100,000–124,999 (*n* = 230)	58.26	36.09	5.65	
125,000–149,999 (*n* = 154)	68.18	28.57	3.25	
150,000–174,999 (*n* = 117)	59.83	35.04	5.13	
175,000–199,999 (*n* = 54)	64.81	29.63	5.56	

Respondents who more frequently elected to have cosmetic procedures done were those aged 25 to 34 years ($p = .002$), residing in the Southern region of the United States ($p = .114$), and had an annual household income of $50,000–74,999 ($p = .162$). Overall, physicians were more commonly selected by patients to conduct cosmetic procedures than nonphysician providers.

required to obtain a 10th grade equivalence of education, complete 300 hours of skin care education at an accredited cosmetology school, and pass an end-of-training examination issued by the State Board of Cosmetology with no continuing education requirements. Requirements for estheticians may fluctuate per state, but do so only minimally.[6] Physician assistants are required to obtain a baccalaureate/bachelor's degree, graduate from an accredited 2 to 2½ years of PA program, pass the Physician Assistants National Certifying Examination to become certified for practice, and fulfill continuing education requirements by completing 100 hours of education credits per 2 years and passing a recertification examination every 10 years.[7]

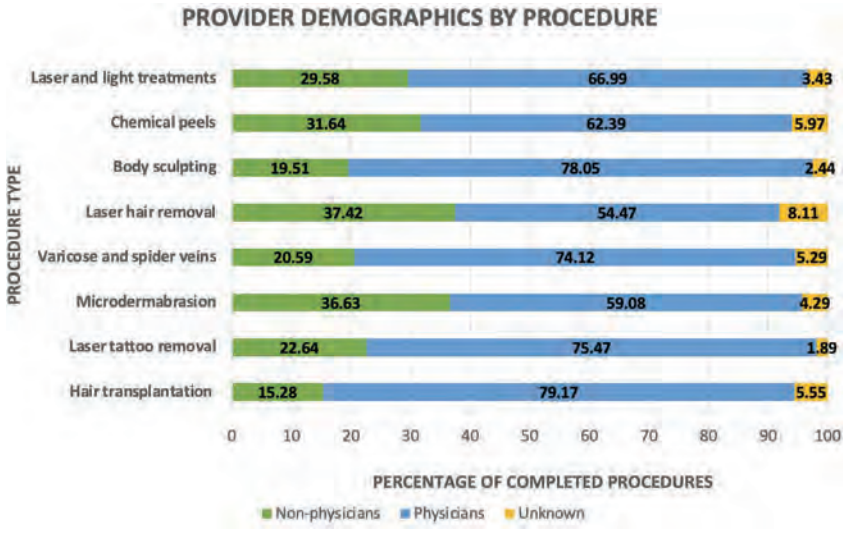


Figure 1. Provider licensing demographics with respect to procedure. Although all procedures were more frequently performed by physicians, approximately one-third of laser and light treatments, chemical peels, laser hair removal treatments, and microdermabrasions were completed by nonphysician providers.

ATTACHMENT D

TABLE 2. Patient-Reported Reasons for Choosing Physician or Nonphysician Providers for Cosmetic Procedures

	Physician, %	Nonphysician, %	Unsure, %
Referral from a physician	66.81	25.73	7.46
Referral from a friend	55.70	36.69	7.60
Being affiliated with a professional organization	65.72	28.09	6.19
The specialty in which the physician is board-certified	67.81	26.52	5.67
The level of licensure of the practitioner (i.e. physician, nurse, physician assistant, and cosmetologist)	59.77	34.10	6.13
The location of the practitioner	59.14	35.80	5.06
Physician or practice website	73.14	24.00	2.86
Being a pioneer in the field	75.00	24.22	0.78
Before-and-after photographs	59.83	32.05	8.12
Number of procedures performed by the practitioner	56.46	40.82	2.72
Price	42.50	47.50	10.00

The most frequently cited reasons that patients selected a physician were the physician's reputation as a "pioneer" in the field, the physician's or practice website, and the physician's specialty. Patients most commonly reported selecting nonphysician providers because of price, number of procedures performed by the provider, and referrals from friends.

Although overlap of educational content may occur between different types of providers, greater quantity and quality of research demonstrates improved patient outcomes and avoided medical emergencies. Furthermore, in a study investigating who pioneered the field of cosmetic procedures, dermatologists were found to be the top contributors to most cosmetic procedures.[8] Furthermore, one study examined the impact of an additional seminar in caring for asthmatic patients. Pediatricians who completed the seminar more frequently appropriately prescribed corticosteroid treatments and provided adequate patient education than physicians who did not attend the seminar, resulting in significantly fewer symptoms, necessary follow-up visits, crises requiring emergency medical attention, and hospitalizations.[9] Given the significant improvement that even a single seminar of further medical education provided to better patient outcomes, longer and consequently more thorough educational requirements for cosmetologists, as similarly mandated of physicians, could be key to ensuring patient safety and satisfaction with cosmetic procedures.

Although the study data demonstrates that physicians continue to more frequently perform all surveyed procedures, approximately one-third of laser and light treatments, chemical peels, laser hair removal treatments, and microdermabrasions are, concerningly, outsourced to nonphysician providers. In a survey completed by the ASDS, physicians reported that 61% to 100% of their complication treatments stemmed from procedures completed at medical spas, which are more likely to employ nonphysician providers such as estheticians or cosmetologists.[10] Furthermore, quantitative evidence supported that the most common treatments leading to complications were laser hair removal treatments, fillers, and intense pulsed light.[10] Although one-third of laser hair removal is performed by nonphysicians, Jalian and colleagues[11] reported that 75.5% of hair removal lawsuits from 2004 to 2012 were performed by nonphysicians. Allowing for nonphysician providers to perform treatments evidenced to more frequently lead to complications requiring physician treatment (i.e. laser treatments) at such a high frequency and without guideline change is likely to worsen patient safety prospects moving forward. The ASDS study concluded that 58.8% of the physicians categorized procedures completed at medical spas to be "very" or "extremely" endangering towards patient safety, with 95.8% of the physicians desiring stricter regulations on procedures available at medical spas.[10] In addition to more thorough education requirements, stricter regulations can doubly serve as a line of defense against complications arising from cosmetic procedures.

Although moderate adverse complications were more likely to occur when procedures were performed by a nonphysician in comparison with a physician provider, approximately 70% of respondents believe that nonphysicians are qualified to complete cosmetic procedures. These results may reflect either an unawareness of complication frequency in relation to licensing status of providers or the growing sentiment that nonphysician providers can provide care that is a satisfactory substitute for physician care. In a 2016 study investigating patient perceptions about nurse practitioners in comparison to physicians, patients reported

feeling that nurse practitioners were more holistic in their care.[12] Furthermore, patients reasoned that picking a provider with more experience was more important during selection than provider type, thus influencing patients to pick nurse practitioners who fit these conditions.[12] As such, the current cosmetic landscape has begun to shift toward patients more commonly selecting nonphysician providers for completion of cosmetic procedures.

Factors that may influence whether respondents choose physicians or non-physician providers included sex and procedure costs. As found in the study results, men were more likely to see physicians than nonphysician providers for cosmetic procedures, possibly because of who is more likely to provide referrals. An interview study found that men often underuse health care services because of the societal pressure for men to appear invulnerable, immune, and without need for help.[13] The findings implicate that men may choose to confide directly in physicians for referrals of cosmetic procedures to avoid demonstrating help-seeking behavior in their personal social circles. As physicians are more likely to refer to other physicians or nonphysician providers within their own practice, men may be choosing to see physicians more often than nonphysician providers for cosmetic procedures simply because of who they have asked for advice. However, no confirmatory data are currently available. Price also plays a large role in the choosing of a provider. As shown by the normality of medical tourism, a phenomenon in which patients will seek to complete cosmetic or health procedures outside of one's own home country in favor of cheaper costs despite the many risks (i.e. infection), patients may choose nonphysician providers for lower prices.[14]

Limitations of the study included self-reporting bias and recall of events, as well as patient subjective judgment of severity of adverse outcomes of cosmetic procedures (i.e. mild, moderate, or severe).

Findings of this study support that patient safety is more compromised when nonphysician providers, rather than physicians, complete cosmetic procedures. As respondents indicated in this survey, more rigorous training for nonphysician providers performing cosmetic procedures, ensuring a physician is readily available to reverse complications, or limiting the scope of practice for nonphysician providers may be essential for preventing adverse events. On a consumer level, having more accessible information explaining the differences of training, experience, and qualifications between physicians and nonphysician providers may allow consumers to more accurately perform cost–benefit analyses when deciding on a practice.

Conclusion

The surge in popularity of cosmetic procedures is currently being met by an increase of nonphysician providers completing cosmetic procedures in addition to physicians. However, adverse effects that occur under the care of a nonphysician provider tend to be more severe than adverse outcomes that occur under physicians. Although people may ultimately choose to have procedures done by nonphysicians because of referrals or reduced costs, patient safety and satisfaction should always remain the utmost priority, which may necessitate encouraging people to make an informed decision when choosing a provider.

Acknowledgments

The authors would like to thank the American Society for Dermatologic Surgery—Future Leaders Network and staff for their support in this project, including Tamika Walton, Kristin Hellquist, and Katherine Duerdoth.

In addition, the authors extend their appreciation to the Deputyship for Research & Innovation, Ministry of Education in Saudi Arabia for funding this research work through the project no. IFKSUOR3-606-1.

References

1. American Society for Dermatologic Surgery. *2018 ASDS Survey on Dermatologic Procedures*. Available from https://www.asds.net/medical-professionals/practice-resources/asds-survey-on-dermatologic-procedures. Accessed October 15, 2022.
2. American Society for Dermatologic Surgery. *2019 ASDS Survey on Dermatologic Procedures*. Available from https://www.asds.net/medical-professionals/practice-resources/asds-survey-on-dermatologic-procedures. Accessed October 15, 2022.
3. Valiga A, Albornoz CA, Chitsazzadeh V, Wang JV, et al. Medical spa facilities and nonphysician operators in aesthetics. *Clin Dermatol* 2022;40:239–43.
4. Rossi AM, Wilson B, Hibler BP, Drake LA. Nonphysician practice of cosmetic dermatology: a patient and physician perspective of outcomes and adverse events. *Dermatol Surg* 2019;45:588–97.
5. Thompson AE. JAMA patient page. A physician's education. *JAMA* 2014;312:2456.
6. Pennsylvania Department of State. Pennsylvania licensure requirements. Available from https://www.dos.pa.gov/ProfessionalLicensing/BoardsCommissions/Cosmetology/Pages/Esthetician-Licensure-Requirements-Snapshot.aspx. Accessed October 15, 2022.
7. American Academy of Physician Associates. Become a PA. Available from https://www.aapa.org/career-central/become-a-pa/. Accessed October 15, 2022.
8. Bangash HK, Eisen DB, Armstrong AW, Nelson AA, et al. Who are the pioneers? A critical analysis of innovation and expertise in cutaneous noninvasive and minimally invasive cosmetic and surgical procedures. *Dermatol Surg* 2016;42:335–51.
9. Clark NM, Gong M, Schork MA, Evans D, et al. Impact of education for physicians on patient outcomes. *Pediatrics* 1998;101:831–6.
10. Wang JV, Albornoz CA, Goldbach H, Mesinkovska N, et al. Experiences with medical spas and associated complications: a survey of aesthetic practitioners. *Dermatol Surg* 2020;46:1543–8.
11. Jalian HR, Jalian CA, Avram MM. Increased risk of litigation associated with laser surgery by nonphysician operators. *JAMA Dermatol* 2014;150:407–11.
12. Zhang J, Han Z, Jia M, Guo J, et al. Application effect of doctor-nurse-patient integration model based on heart rate management strategies in middle-aged and young outpatients with hypertension. *Comput Math Methods Med* 2022;2022:7459518.
13. Tudiver F, Talbot Y. Why don't men seek help? Family physicians' perspectives on help-seeking behavior in men. *J Fam Pract* 1999;48:47–52.
14. Pavli A, Maltezou HC. Infectious complications related to medical tourism. *J Trav Med* 2021;28:taaa210.

Aesth Plast Surg (2018) 42:498–510
https://doi.org/10.1007/s00266-017-1063-0

ATTACHMENT D

REVIEW NON-SURGICAL AESTHETIC

Treatment of Soft Tissue Filler Complications: Expert Consensus Recommendations

Fernando Urdiales-Gálvez[1] · Nuria Escoda Delgado[2] · Vitor Figueiredo[3] · José V. Lajo-Plaza[4] · Mar Mira[5] · Antonio Moreno[6] · Francisco Ortíz-Martí[7] · Rosa del Rio-Reyes[8] · Nazaret Romero-Álvarez[9] · Sofía Ruiz del Cueto[5] · María A. Segurado[10,11] · Cristina Villanueva Rebenaque[12]

Received: 25 September 2017 / Accepted: 17 December 2017 / Published online: 5 January 2018

Abstract

Background Dermal fillers have been increasingly used in minimally invasive facial esthetic procedures. This widespread use has led to a rise in reports of associated complications. The aim of this expert consensus report is to describe potential adverse events associated with dermal fillers and to provide guidance on their treatment and avoidance.

Methods A multidisciplinary group of experts in esthetic treatments convened to discuss the management of the complications associated with dermal fillers use. A search was performed for English, French, and Spanish language articles in MEDLINE, the Cochrane Database, and Google Scholar using the search terms "complications" OR "soft filler complications" OR "injectable complications" AND "dermal fillers" AND "Therapy". An initial document was drafted by the Coordinating Committee, and it was reviewed and modified by the experts, until a final text was agreed upon and validated.

Results The panel addressed consensus recommendations about the classification of filler complications according to the time of onset and about the clinical management of different complications including bruising, swelling, edema, infections, lumps and bumps, skin discoloration, and biofilm formation. Special attention was paid to vascular compromise and retinal artery occlusion.

Conclusions Clinicians should be fully aware of the signs and symptoms related to complications and be prepared to confidently treat them. Establishing action protocols for emergencies, with agents readily available in the office, would reduce the severity of adverse outcomes associated with injection of hyaluronic acid fillers in the cosmetic setting. This document seeks to lay down a set of recommendations and to identify key issues that may be useful

✉ Fernando Urdiales-Gálvez
furdiales@institutomedicomiramar.com

[1] Instituto Médico Miramar, Paseo de Miramar 21, 29016 Málaga, Spain

[2] Centro de Medicina Estética Dra Escoda, Rambla de Catalunya 60, Barcelona, Spain

[3] Clínica Milénio, R. Manuel da Silva Leal 11C, Lisbon, Portugal

[4] Centro Médico Lajo-Plaza, Calle Moreto 10, Madrid, Spain

[5] Clínica Mira + Cueto, Av. de Concha Espina 53, Madrid, Spain

[6] Clínica Oftalmológica Antonio Moreno, Calle Esperanto, 19, 29007 Málaga, Spain

[7] Teknobell Médicina Estética, Av. Pdte Carrero Blanco 14, Seville, Spain

[8] Grupo de Dermatología Pedro Jaén, Calle Cinca 30, Madrid, Spain

[9] Clínica de Medicina Estética Dra. Nazaret Romero, Paseo Castellana 123, Madrid, Spain

[10] SClinic, Claudio Coello 92, Madrid, Spain

[11] Hospital del Sureste Vía Verde, Ronda del Sur 10, Arganda del Rey, Madrid, Spain

[12] Clínica de Medicina Estética Dra Villanueva, Carrer de Calvet 10, Barcelona, Spain

for clinicians who are starting to use dermal fillers. Additionally, this document provides a better understanding about the diagnoses and management of complications if they do occur.

Level of Evidence V This journal requires that authors assign a level of evidence to each article. For a full description of these Evidence-Based Medicine ratings, please refer to the Table of Contents or the online Instructions to Authors www.springer.com/00266.

Keywords Esthetic procedures · Dermal fillers · Complications · Treatment

Introduction

Dermal fillers have been injected with increasing frequency over the past three decades for soft tissue augmentation by volume expansion in the management of the aging face. Over the past several years, the number of procedures involving soft tissue fillers has increased from 1.6 million per year in 2011 to more than 2.4 million in 2015 [1].

The growing use of dermal fillers, specifically the use of hyaluronic acid (HA), can be explained by their effectiveness and versatility as well as their favorable safety profiles.

Although the incidence of complications is low and the majority of adverse events are mild, the increase in the number of procedures has produced the concurrent increase in the number of complications [2–4]. Among these, serious occurrences are fortunately rare, although probably underreported.

It is noteworthy that proper selection and placement of product can help avoid some complications [5].

The classification of filler complications can be divided according to severity (mild, moderate, or severe); nature (ischemic complications and non-ischemic); or by the time of the onset (early or late) [6, 7]. A classical classification proposed by Rohrich et al. [8] suggested that complications should be classified as early, late, and delayed, roughly defined as less than 14, 14 days to 1 year, and more than 1 year, respectively, as these time frames correlate well with the potential underlying etiology. Although the panel proposes to classify filler complications as immediate onset (up to 24 h after procedure); early onset (24 h to 4 weeks); and delayed onset (more than 4 weeks), to facilitate the understanding and follow-up of the manuscript, the immediate- and the early-onset complications have been listed together.

Although different papers about the management of dermal filler complications have emerged in the last years [2–4, 6, 7, 9–13], optimal complication management remains an unmet need in the field of esthetic medicine.

This paper aims to describe potential adverse events associated with dermal fillers and to provide guidance on their treatment and avoidance.

Methods

On November 2016, a multidisciplinary group of experts in esthetic treatments, selected based on their level of expertise in this subject, convened to discuss the management of the complications associated with dermal fillers use. Among the different topics discussed in the meeting, the classification of the filler complications and the management of such complications have emerged as key issues. The authors developed this consensus paper based on those discussions and a review of the current literature.

Searches of MEDLINE (from 2000 to November 2016), the Cochrane Database (from 2000 to November 2016), and Google Scholar were conducted using the search terms “complications” OR “soft filler complications” OR “injectable complications” AND “dermal fillers” AND “Therapy”. References cited in selected articles were also reviewed to identify additional relevant reports. Limits were set for articles written in English, French, and Spanish with human subjects. Additional data were identified through bibliographic reviews. Additionally, relevant published national and international guidelines were also scrutinized.

Because of the nature of esthetic procedures, which are usually elective processes, it is not easy to devise meaningful prospective clinical trials that evaluate complications. There are a few prospective trials, but these are often not randomized or controlled. Therefore, our knowledge base mainly comprised case reports and summaries of individual practitioner’s experience.

An initial document was drafted by the Coordinating Committee, and it was reviewed by the expert panel members. The Coordinating Committee evaluated the panel’s comments and modified the draft as they considered necessary. Subsequent revisions were based on feedback from the other authors until a consensus was achieved, and the final text was then validated (Fig. 1).

The recommendations expounded in this document represent the panel’s expert opinion based on their clinical experience as well as on published data regarding dermal filler complications in esthetic procedures.

Results

According to the time of onset, the panel proposes to classify filler complications as immediate onset (up to 24 h after procedure); early onset (24 h to 4 weeks); and

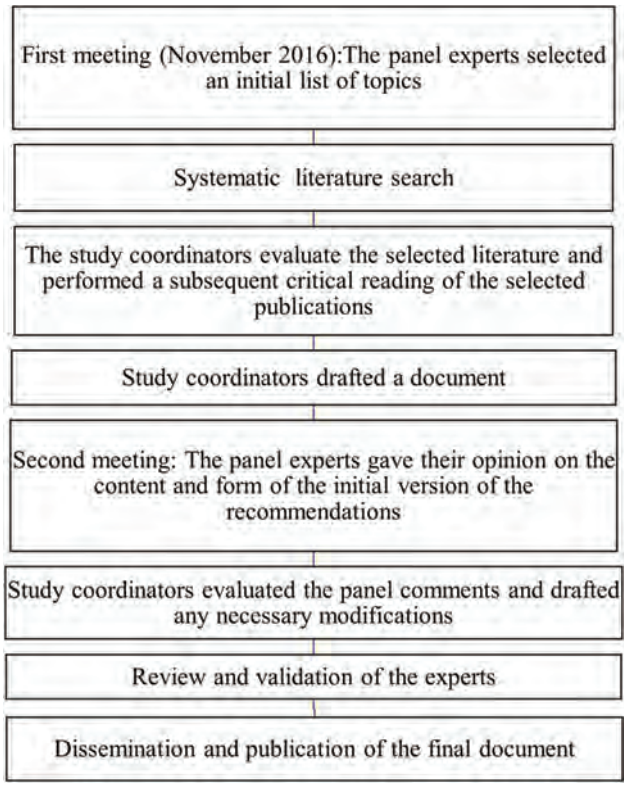


Fig. 1 Flow diagram of the consensus process

delayed onset (more than 4 weeks). Nevertheless, to make the manuscript reading more pleasant, the immediate- and the early-onset complications have been listed together. The main types of adverse events by time of onset are illustrated in Table 1.

Immediate- and Early-Onset Dermal Filler Complications

Bruising/Ecchymosis

Bruising is an understandable and common complication, though unwelcome by patients, of filler injections. Bruising is observed more frequently after injection into the dermal and immediate subdermal planes using fanning and threading techniques [14].

Bruising may be treated with cold compresses after the procedure, arnica, aloe vera, or vitamin K creams [6, 15, 16]. The risk of bruising may be reduced by injecting the filler slowly. If bruising appears, it can be reduced by pressing with a compress [2].

Different substances associated with anticoagulation including nonsteroidal anti-inflammatory drug medications, many vitamin/herbal supplements, and antiplatelet should be discontinued 7–10 days (not without consultation with the treating physician) prior to treatment to reduce the risk of bruising [2, 16, 17].

Clinical studies evaluating the risk of bleeding in patients undergoing minor dental surgery procedures have reported conflicting results. Several studies reported that the postoperative bleeding rate in patients undergoing oral anticoagulant treatment, such as warfarin or coumadin, was not higher than that in patients not undergoing oral anticoagulant treatment [18–20]. However, some studies have reported more postoperative bleeding in oral anticoagulant treated patients [21, 22]. The results of a recently published meta-analysis found that although patients treated with oral anticoagulants have a higher postoperative bleeding risk than those not treated with oral anticoagulants following minor dental surgery, local hemostatic methods effectively stopped the bleeding [23].

An expert group consensus report, focused on preventing dermal fillers complications, recommended to reduce the risk of bruising and to pay special attention in patients taking oral anticoagulants [24].

In summary, the risk of bleeding in patients taking oral anticoagulant treatments and with a stable international normalized ratio (INR) in the therapeutic range 2–4 is really small, and its discontinuation may increase the risk of thrombosis [25].

According to the panel opinion, if the anticoagulant treatment is well balanced, the associated risk of discontinuing the treatment is greater than that of bleeding.

Although it is not forbidden, it is advisable to avoid strenuous exercise for 24 h to reduce the risk of bruising and swelling [17].

Regarding this issue, the panel recommends:

(a) Prophylaxis: To use arnica with vitamin K creams for 3 to 4 days.
(b) Treatment: To use arnica and vitamin K creams/ photoprotection.

Swelling and Edema

Some transient swelling in the immediate postprocedural period is normal and occurs with all dermal fillers, but may vary in timing and severity depending on the specific product used [6, 16]. Besides injection volume and technique, patient factors, such as dermographism, may also influence the amount of swelling. The most commonly affected areas are the lips and the periorbital region. In patients with a long-lasting lip augmentation procedure a transient swelling of the lips may occur.

It should be mentioned that this swelling should not be confused with an antibody-mediated edema (angioedema), which is extremely rare [19, 26].

The panel recommends:

Table 1 Overview of the adverse events associated with the use of dermal fillers. Adapted from Funt and Pavicic [6]

Adverse events	Signs and symptoms	
	Immediate/early adverse events[b]	Delayed adverse events[c]
Injection site reactions[a]	Erythema	Erythema
	Edema	Edema
	Pain/tenderness	Pain/tenderness
	Bruising	Nodule/abscess
	Itching	Systemic responses
		Biofilm
Infection	Erythema	Biofilm
	Edema	Herpes outbreak
	Pain/tenderness	Foreign-body granuloma[d]
	Acne papule formation	
	Nodule/abscess	
	Herpes outbreak	
Hypersensitivity	Erythema	Migration of filler material
	Edema	
	Pain/tenderness	
	Non-fluctuant nodules	
Technical and placement errors	Bumps/lumps	Immune reactions
	Asymmetries	Compromised muscle function
	Contour irregularities	Dysesthesias and paresthesias
	Compromised muscle function	
	Dysesthesias, paresthesias, and anesthesia	
Skin discoloration	Redness	Persistent discoloration
	Whiteness	Persistent scarring
	Hyperpigmentation	
Vascular compromise[e]	Blurred vision	Tissue necrosis
	Loss of vision	
	Pain	
	Blanching	

[a]Atypical as a delayed adverse events
[b]Occurring up to several days post-treatment
[c]Occurring from weeks to years post-treatment
[d]Varying from subclinical histologic changes to disfiguring nodules
[e]Retinal artery occlusion

(a) Prophylaxis:

i. Anti-inflammatory Enzyme:

1. Wobenzym Vital® (Diafarm, 08210 Barberà del Vallès, Barcelona, Spain): 2 capsules/ 12 h.
2. Bromelain: 300 mg/day, divided in three doses.

ii. Arnica/gelsenium: 4–5 pills/24 h 3–4 days.
iii. Cold compresses (about 5 min).

(b) Treatment:

i. Mild: Cold compresses/anti-inflammatory enzyme (Wobenzym Vital® or Bromelain, according to the previous dosage)/observation.
ii. Moderate:

1. Streptokinase/streptodornase (10,000/2500 U): 2 pills/8 h, for 3–6 days.
2. Nonsteroidal anti-inflammatory drugs (NSAIDs):

Table 2 Different NSAIDs and anti-inflammatory enzyme treatments recommended by the panel

Product	Dose	Comment
Diclofenac 50 mg	1/12 h	Associated with some gastric protector (no more than 5 days)
Varidase	4–8 pills/6 H and after 2 pills/8 h	For 7–10 days and after for 3–6 days
Bromelin 50 mg[a]	4–8 pills/24 h	For 3–6 days
Bromelin, papain, trypsin, and quimotrypsin[b]	4–8 pills/24 h	For 3–6 days
Ibuprofen	400–600 mg/8 h	For 2–3 days
Dexketoprofen trometamol	25 mg/8 h	For 1–3 days
Acetyl salicylic acid	100 mg/24 h	For 7 days (if necrosis)

[a]Fortilase®, MEDA PHARMA SL, Avenida de Castilla, 2. San Fernando de Henares, Madrid. Spain

[b]Wowenzym Vital®; Diafarma Laboratories, 08210 Barberà del Vallès, Bacrelona. Spain

Table 3 Different steroid treatments recommended by the panel

Product	Dose	Comment
Deflazacort[a]	1–1.5 mg/kg/day	For 15–21 days. Associated to some gastric protector
Prednisone 30 mg	1 pill/24 h	For 3 days
	30–60 mg/24 h	For 2–3 weeks (corticoids in decreasing doses)
Methylprednisolone	40–80 mg/24 h	For 2–3 weeks (corticoids in decreasing doses)

[a]Deflazacort is the first-line treatment. The length of the treatment should be from 3 to 6 weeks, prescribing the drug at increasing doses each week; i.e., first week 0.5 mg/kg/day until reaching 1.5 mg/kg/day. Subsequently, corticoids in decreasing doses

- Cox 1: Ibuprofen 400–600 mg/8 h.
- Cox 2: Celecoxib (200–400 mg/24 h).

The different NSAIDs and anti-inflammatory enzyme treatments are summarized in Table 2.

Before prescribing NSAIDs, it is important to consider the following recommendations:

(a) To use the lowest dose and for the shortest time.
(b) To select the NSAID according to the drug profile and the patient risk factors.
(c) To use gastroprotective agents for minimizing the gastrointestinal harm associated with use of NSAIDs.

iii. Severe:

1. Prednisone: 1 mg/kg/day + pantoprazole 40 mg. Approximately for 3 days (according to the clinical course).
2. Deflazacort: 1–1.5 mg/kg/day + pantoprazole 40 mg. Approximately for 3 days (according to the clinical course).
3. In case of necrosis: lymphatic drainage and soft massage.

The different steroid treatments are summarized in Table 3.

Because dermal fillers are essentially foreign bodies, some patients may develop hypersensitivity to injected products due to an immunoglobulin E (IgE)-mediated immune response (Type I hypersensitivity reaction). Angioedema occurs within hours of exposure, although the reactions can be severe and can last for several weeks [27].

This angioedema will usually subside within a few days with antihistamines and/or oral steroids. The patient should be closely monitored to rule out possible infection.

Additionally, delayed hypersensitivity reactions, which typically occur 1 day after injection, are characterized by induration, erythema, and edema, and are mediated by T lymphocytes rather than antibodies [28]. Delayed hypersensitivity reactions are non-responsive to antihistamines. In the case of HA, this will involve treatment with hyaluronidase.

Erythema

Immediately after injection, some skin redness may occur and is normal. Treatments for rosacea may be effective, including oral tetracycline or isotretinoin [6]. A medium-strength topical steroid is advocated for persistent erythema. However, long-term use of high-potency steroids should be avoided. Additionally, vitamin K cream may be useful in accelerating resolution of erythema [29].

Infections

Any procedure that breaks the surface of the skin carries with it a risk of infection, and injecting dermal fillers is no exception. Acute infections, which appear as acute inflammation or abscesses at the site of injection, are typically due to common pathogens present on the skin such as *Staphylococcus aureus* or *Streptococcus pyogenes*.

If untreated, the conditions may lead to sepsis, particularly in elderly people or in patients with other conditions that alter the immune system. Mild forms may be treated with oral antibiotics, while more serious ones require intravenous antibiotics and hospitalization [6, 30].

The panel recommends:

i. Amoxicillin clavulanic acid 4 g/24 h 15 days.
ii. Ciprofloxacin 500–750 mg bid for 2–4 weeks.

The different antibiotics recommended by the panel are listed in Table 4.

Herpetic Outbreak

Dermal filler injections can lead to reactivation of herpes virus infections. The majority of herpetic recurrences occur in the perioral area, nasal mucosa, and mucosa of the hard palate [2, 6, 16, 17].

Patients with a history of severe cold sores (more than 3 episodes) should be prescribed antiherpes medication prophylactically before treatment when injections in vulnerable areas are planned. In these patients, the panel recommends: Valaciclovir 1 g/24 h 1 day before and 3 days after filler injection.

Additionally, according to the panel recommendations, in patients with active herpes lesions, injections should be delayed until their complete resolution.

Dysesthesias, Paresthesia, and Anesthesia

Nerve damage during an esthetic procedure, although very rare, can occur as result of different causes such as direct trauma, injection of filler into the nerve, tissue compression by the product. Nerve injury may be either transient and reversible, or permanent. The most common site of dysesthesias, paresthesia, and anesthesia is the infraorbital nerve. Less commonly, a transient Bell's palsy or marginal mandibular nerve dysfunction has been seen and may last several weeks [2, 6, 16, 17].

Although 71% of patients with Bell's palsy experience complete spontaneous resolution, the remaining 29% exhibit lifelong residual hemifacial weakness. Besides the protective strategies of the ocular surface (artificial tears, occlusion, etc.), the mainstay of acute management of Bell's palsy is a short course of high-dose (for example, 1 mg/kg) oral steroids [31]. Surgical decompression of the meatal segment, antiviral therapy, electrotherapy, physical therapy, and acupuncture has been proposed, though the evidence does not support their use [31].

The panel considers it crucial to have a thorough knowledge of facial anatomy to minimize the incidence of such complications.

Table 4 Different antibiotic treatments recommended by the panel

Product	Dose	Comment
Amoxycillin/clavulanic acid	4 g/24 h	For 10–15 days
Cloxacillin	3 g/24 h	For 10–15 days
	500 mg/8 h	For 30 days
Ciprofloxacin	500 mg/8 h	For 3–6 weeks
Azithromycin	500 mg/24 h	For 3 days
Minocycline	500 mg/12 h	For 30 days
Flucloxacillin	500 mg/8 h	For 7 days

Lumps and Bumps

Lumps and bumps are one of the most common complications associated with filler injections [16]. They can be classified according their type (non-inflammatory, inflammatory, or infectious) as well as their time to presentation (early, late, or delayed) [8]. As they can arise from a number of causes, investigation may be required to establish a diagnosis. As a general rule, early lumps and bumps present within days or weeks, tend to be painless, and are most likely the result of suboptimal techniques such as excess filler use, superficial placement, and incorrect product for the indication [16, 32]. Lumps occurring in the early post-treatment period may respond to massage.

The panel recommends:

(a) Observation: do not treat if the inflammation is improving.
(b) If the non-inflammatory lump persists, treat the over correction:

i. Needle aspiration or minimal stab wound incision with evacuation.
ii. Hyaluronidase 150U/mL (be aware of possible allergic reactions).
iii. To treat the post-inflammatory hyperpigmentation: intense pulsed light/laser; photo-protection; or depigment cream.

Hyaluronidase preparation, dilution, and doses are summarized in Table 5.

Table 5 Hyaluronidase preparation, dilution, and doses recommended by the panel

Dilution	Dose
150 IU/mL saline	150 IU/mL
1×10^4 μg in 3 mL (saline)	0.3–0.5 mL per injected point
1×10^3 IU in 2–4 mL (saline)	50–200 IU in nodules
1.5×10^3 IU in 10 mL (saline)	500–1.000 IU in patients at risk of necrosis
	100–200 IU 3–4 mm in depth[a]

[a]This strategy refers to the injection of hyaluronidase throughout the area around the vascular occlusion point to promote its intravascular penetration and facilitate removal of the HA that is obstructing the vessel

Table 6 Strategies for reducing the risk of skin necrosis with hyaluronic acid fillers

Panel recommendations
a. Aspirating prior to injection
b. Utilizing lower volumes and serial injections in high-risk areas
c. Treating one side at a time
d. Pinching/tenting the skin to provide more space superficial to the branches of the main arteries
e. Manual occlusion of the origin of the supratrochlear vessels with the non-dominant finger
f. Blunt cannulas may reduce, but not eliminate, the risk

Vascular Compromise

Vascular compromise after a soft tissue filler injection is a major, immediate complication that is almost always the result of intravascular injection into an artery, causing an embolism that impedes blood flow.

The incidence of intravascular injection seems to be more frequent than we assumed. The results of an internet-based survey conducted on 52 experienced injectors worldwide showed that a 62% of them reported one or more intravascular injections [32]. Recognition of a vascular event and swift and aggressive treatment is necessary to avoid potentially irreversible complications [33–36].

The two primary diagnostic symptoms of vascular occlusion are pain and changes in skin color. Arterial occlusion is typified by immediate, severe, and disproportionate pain and color changes (white spots) [32], whereas venous occlusion may be associated with less severe, dull, or delayed pain (in some cases there may be no pain).

Because intravascular occlusions are rare events, present recommendations for prevention and management are based almost exclusively on expert opinion [37] and consensus reports [6, 16, 17, 38].

Nevertheless, when vascular occlusion is suspected, it is crucial that the injection is stopped immediately and treatment is rapidly instigated. The objective is to facilitate blood flow to the affected area. Treatment strategies include hyaluronidase, warm compress, massaging or tapping the area, and applying 2% nitroglycerin paste to promote vasodilatation [32, 39, 40].

Hyaluronidase should be injected immediately, regardless of the filler used, and administered daily in liberal doses where signs and symptoms are present [6, 16, 17, 38].

For intravascular infarction, high doses of hyaluronidase (200–300 U) have been recommended, [16, 17, 38]. When injecting hyaluronidase to treat acute ischemia, consensus recommendations are that the entire ischemic area be treated, not just the site where HA was originally injected [16, 17, 38]. If there is no improvement, the procedure should be repeated hourly until clinical resolution is achieved [16]. Doses up to 1500 U may be required to achieve reversal of vascular compromise [16, 17, 38].

The risk of an intravascular injection can be reduced by different strategies, which are listed in Table 6.

Retinal Artery Occlusion

The occlusion of the central retinal artery (CRA), or some of its branches, is a rare but devastating visual complication that can occur after an esthetic procedure with soft tissue fillers, such as autologous fat, hyaluronic acid, or collagen [41].

A literature review published in 2015 reported 98 cases of vision changes following filler injection [42]. The injection sites identified with higher risk of complications were the glabella (38.8%), nasal region (25.5%), nasolabial fold (13.3%), and forehead (12.2%) [42]. As regards, the filler type, autologous fat, was the most common causative material (47.9%) followed by hyaluronic acid (23.5%) [42].

The underlying mechanism of action leading to vision loss is retrograde flow [42, 43]. If the tip of the needle penetrates the wall of a distal branch of ophthalmic artery,

the force of injection can expand arterioles and cause retrograde flow [42, 43]. Although this is the prevailing theory regarding the mechanism of occlusion, theories related to compression of vessels may also contribute [43].

The main symptom is blindness in the affected eye, usually painless, which can occur within seconds after injection. Other associated symptoms are pain at the injection site and headache [41–44].

If visual loss has occurred, therapeutic measures should be immediately implemented, because maintained CRA occlusion for more than 60–90 min causes irreversible blindness [45].

The therapeutic measures that have to be performed at the center where the procedure was made would be:

- Medical treatment [43]:
    - One drop of topical timolol 0.5% and/or an acetazolamide 500 mg tablet (after excluding allergy to sulfonamides).
    - To administer a sublingual pill (325 mg) of acetylsalicylic acid or one of nitroglycerin 0.6 mg.
    - To administer an intravenous infusion, 100 mL over 30 min, of mannitol 20%.
- Digital massage [43]: It should start immediately while preparing the treatment and to continue once the drugs have been administered.
    - The patient should be placed in a supine position.
    - Ensure the patient's eyes are closed.
    - Apply firm pressure (enough to ensure that the eyeball is indented about 2–3 mm) on the eyeball through the closed eyelids.
    - Apply firm pressure for 5–15 s and quickly release.
    - Repeat this cycle for at least 5 min.

If despite these measures the patient does not recover the vision in the first 15–20 min, the patient must be referred to an ophthalmology-specialized center for performing an anterior chamber paracentesis for decreasing intraocular pressure [43].

Because, up to now, fibrinolytic or hyaluronidase infiltrations have not demonstrated an unequivocal efficacy; their use is not widespread [43].

Due to the seriousness of the complication, prevention through a good understanding of facial vasculature anatomy and injection techniques is extremely important.

Late-/Delayed-Onset Dermal Filler Complications

Bruising

Although bruising is usually an early-onset complication, persisting staining may arise. Larger or cosmetically distressing purpura can be treated with vascular lasers, either pulsed dye light or potassium titanyl phosphate lasers, to speed recovery [6, 16].

Edema

Angioedema Angioedema typically has an early onset; however, episodes that last more than 6 weeks may be observed. These cases are often difficult to treat and have a variable response to medication. The therapeutic approach is stepped, moving to the next step if an inadequate response was obtained. Edema should be controlled with the smallest dose of oral steroids that is effective [6]. Additional treatment options including topical or intralesional steroids, or immunosuppressive agents, have been proposed [2].

Non-Antibody-Mediated (Delayed) Edema Delayed hypersensitivity reactions, which are characterized by induration, erythema, and edema, usually occur 1 day after injection, but may be seen as late as several weeks after injection and may persist for many months [46].

Antihistamines are not effective in these reactions. The best approach is to remove the allergen. If HA had been used, treatment with hyaluronidase would be recommended. Other fillers may require treatment with steroids until the filler resorbs, laser treatment, and/or extrusion [47]. Sometimes, it is even necessary to make, as a last resort, an excision.

Malar Edema Malar edema is a particularly serious complication that has been frequently reported with all fillers when injected into the infraorbital hollow and tear troughs [48].

The phenomenon of malar edema can be explained by an understanding of the anatomy of the lower eyelid. Injection of fillers may cause edema by either augmenting the impermeable barrier of the malar septum (impeding lymphatic drainage) or bydirect pressure on the lymphatics when injection volumes are too large [48].

It is worth mentioning that malar edema is long lasting and responds poorly to treatment. The therapeutic strategies include head elevation, cold compresses, manual compression multiple times daily, lymphatic drainage, and methylprednisolone. In those patients treated with HA, hyaluronidase treatment should be given [48].

Nevertheless, the best approach is to reduce its incidence by patient and filler selection; limiting filler volume; and by placing filler material deep into the malar septum at the immediate pre-periosteal level [48].

Persistent periorbital edema can be observed when injecting too much volume in the tear trough or when the product is placed too superiorly and too superficially. This complication is more frequent in patients with preexisting malar edema, because the obstruction of lymphatic drainage may be an inciting factor [16].

Skin Discoloration

Neovascularization The tissue trauma caused, as a result of tissue expansion and/or by excessive molding and massage of the filler, can favor the appearance of new capillaries, arterioles, and venules. Neovessels may appear days or weeks after the procedure, but should fade within 3–12 months without further treatment. Laser treatment has shown to be effective in these cases.

Hyperpigmentation Hyperpigmentation is not an uncommon complication in dermal filler procedures, especially in subjects with Fitzpatrick skin types IV–VI, although post-injection hyperpigmentation can also be seen in other skin types [49, 50].

For managing this problem, the first therapeutic approach should be with a bleaching agent such as topical hydroquinone (2–8%) and Retin-A (tretinoin) combined with daily full-spectrum sunscreen application [6]. In those cases of resistant post-inflammatory hyperpigmentation, chemical peels may also be used. If the treatment is not successful, the next steps include the treatment with intense pulsed light, a pulsed dye laser, or fractional laser [6].

Tyndall Effect When particulate HA fillers are inappropriately implanted into the superficial dermis or epidermis they cause a bluish hue referred to as "Raleigh scattering" or the "Tyndall effect" [51]. If not treated, superficial product has been commonly observed to last for very long periods of time, even years [16].

Hyaluronidase should be the initial approach to treatment. For those patients who do not achieve a good response, dyspigmentation can be treated by nicking the skin with a small-gauge needle or surgical scalpel and expressing the superficial, unwanted dermal filler [52, 53]. This therapeutic strategy may be applied immediately, or as long as 12 months or more after injection [53].

Infection

Delayed-onset chronic infections, which generally develop 2 or more weeks after injection, tend to affect a more generalized area and may involve an atypical organism (such as *Mycobacteria* or *Escherichia coli*). These are challenging for both diagnosis and treatment and can cause a chronic inflammatory response.

In the opinion of the panel, a sequence of treatment options similar to that in early acute infection should be followed:

(a) To perform a bacterial culture and clinical assessment to decide type of infection and treat with antibiotics or corticosteroids.
(b) It is important to do a differential diagnosis with hypersensitivity, as the use of steroids should be avoided in infection.
(c) There are not comparative studies supporting the effectiveness of a specific therapeutic regimen. Once the species is identified, an antibiogram is required. If atypical mycobacteria are suspected, while waiting for the antibiogram results, an empirical treatment with antibiotics, which cover atypical mycobacteria, such as claritromicina 500 mg/twice daily combined with ethambutol or rifampicin, may be recommended.

Abscess Abscess formation is a rare complication, reported in permanent hydrogel fillers, occurring any time from 1 week to several years after treatment; it may persist for weeks, and periodically recur for months.

The first-line therapy is drainage and antibiotics. As mentioned for the delayed-onset chronic infections, the panel recommends, in order to tailor the treatment, to obtain bacterial cultures and perform sensitivity reports [54]. Although it is extremely rare, midfacial and periorbital infection may result in intracerebral complications [6].

It has been proposed that low-grade infections are responsible for all delayed-onset complications, including foreign-body granulomas, as a result of biofilm formation [55].

Nodules

Nodules and lumps are common complications resulting from the use of dermal fillers.

Nodules must be categorized as inflammatory or non-inflammatory.

Inflammatory Nodules Delayed-onset nodules (from 4 weeks to 1 year or even longer) are usually inflammatory (immune responses to the filler material) and/or infection related (including biofilm) [56, 57].

Biofilms are widespread in nature and consist of densely packed communities of bacteria that surround themselves with secreted polymers. However, in patients presenting

delayed inflammatory complications due to permanent filler, biofilm gained much interest after demonstrating that bacteria could be detected in biopsies, although a culture test had frequently been negative [58]. It is therefore important to use molecular techniques, such as polymerase chain reaction or fluorescence in situ hybridization tests for delayed-onset nodule complications where biofilm involvement is suspected [56].

It may be extremely difficult to distinguish inflammation due to a bacterial biofilm from a low-grade hypersensitivity reaction.

Many bacterial species form biofilms, and as biofilms progress, they become more antibiotic and culture resistant. As regards treatment, although these infections are difficult to treat, the cure is removal of the implant, which is not always possible. In those cases of HA fillers, hyaluronidase can be used. However, we must be extremely cautious because, according to the labeling, hyaluronidase should not be used in the presence of an active infection (cellulitis) as it may facilitate the spread of infection into adjacent tissues [37].

Other strategies for treating biofilm include low doses of triamcinolone mixed with 5-fluorouracil (FU) (0.1 mL triamcinolone 40 mg/mL and 0.9 mL 5-FU 50 mg/mL) injected at regular (weekly × 2, once every 2 weeks × 2, then monthly) intervals until resolution is achieved [16]. Although the reason for the therapeutic success of 5-FU remains unknown, it has been suggested that it interacts with AriR, a regulatory gene that inhibits the formation of biofilm [59].

Additionally, we have evidence supporting the use of human platelet-rich plasma in the area of the biofilm infection, with a triple effect intention: antimicrobial; for favoring HA degradation of the inflamed tissues; and to destroy the biofilm [60–62].

Regarding antibiotic treatment, a consensus report on prevention and management of HA complications recommended the following empiric antibiotic scheme: clarithromycin 500 mg plus moxifloxacin 400 mg twice daily for 10 days, or ciprofloxacin 500–750 mg twice daily for 2–4 weeks, or minocycline 100 mg once daily for 6 months [17].

Foreign-Body Granulomas Foreign-body granulomas may form as the body's immune system responds to a foreign body that cannot be broken down by the usual mechanisms.

Although they can occur with all injectable dermal fillers, the incidence is very rare (from 0.01 to 1.0%) and usually appears after a latent period, which can be several months to years after injection [63, 64]. Diagnosis of granulomas is further complicated by the fact that clinicians are sometimes faced with patients with unknown or incomplete medical and cosmetic treatment history.

Granulomatous reactions to hyaluronic acid fillers can be treated with hyaluronidase with the dosing of 150 U/mL.

Once infection has been ruled out or quiescent, granulomas may respond to oral or intralesional steroids. If steroids are not enough, many patients will respond to the addition of 5-FU to the corticosteroids. In cases of repeated failure of other therapies, surgical excision is the treatment of choice for foreign-body granuloma [2, 6, 16, 17].

Tissue Necrosis

Impending tissue necrosis, although fortunately rare, may occur as a result of inadvertent injection of filler into vessels supplying the mucosa or the skin, resulting in vessel occlusion. On the other hand, necrosis may also occur secondary to local edema or to occlusion of adjacent vasculature secondary to the hydrophilic properties of the product [65, 66].

The risk of skin necrosis can be reduced by different strategies (see Table 6).

All the injectors have to be familiar with the signs of skin necrosis and the appropriate therapy. For intravascular infarction, the panel recommended:

(a) To apply a warm gauze, tapping the area to facilitate vasodilatation, and massage of the area.
(b) To use topical nitroglycerin (1 or 2%) paste 2 or 3 times/daily in the office and at home by the patient. Nitroglycerin sublingual tablets can be used.
(c) Hyaluronidase injection (200–400 IU/1–2 mL) + massage. See Table 5.
(d) Although it was not absolutely proved, it was stated that acetylsalicylic acid (500 mg/8 h, 24–48 h) might be helpful.
(e) If there are ocular symptoms (blurred vision, loss of vision, or ocular pain), the patient has to be urgently referred to the ophthalmologist.
(f) Other strategies including systemic or topical steroids (prednisone 20–40 mg each day for 3–5 days), low molecular weight heparin, hyperbaric oxygen, sildenafil (1 per day for 3–5 days) have been proposed [17, 67, 68].

Conclusions

Because of their efficacy and safety, esthetic procedures with dermal fillers have become increasingly popular. However, although the incidence of complications is relatively low and the majority of adverse events are mild, the

increase in the number of procedures has been accompanied by a concurrent increase in the number of complications. As optimal complication management remains an unmet need in the field of esthetic medicine, minimizing their incidence by means of appropriate patient, product, and injection technique selection, as well as a sound understanding of facial anatomy, is probably the best approach.

Clinicians should be fully aware of the signs and symptoms related to complications and be prepared to confidently treat them. Establishing action protocols for emergencies, with agents readily available in the office, would reduce the severity of adverse outcomes associated with injection of hyaluronic acid fillers in the cosmetic setting.

It is our hope that this article will help clinicians, who are just starting to use dermal filler procedures, to effectively manage their potential complications.

Acknowledgements The authors wish to thank Allergan Laboratories for their collaboration with the logistics of the meetings and the assistance with the medical writing. The authors thank Antonio Martinez (MD) of Ciencia y Deporte S.L. for providing medical writing and editorial assistance. It should be noted that Allergan S.A. was not involved in the preparation of the recommendations nor did the company influence in any way the scientific consensus reached.

Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflicts of interest to disclose.

References

1. American Society of Plastic Surgeons: 2014 Plastic surgery statistics report. Available at: http://www.plasticsurgery.org/Documents/news-resources/statistics/2014-statistics/plastic-surgery- statistics-full-report.pdf. Accessed December 26, 2016
2. De Boulle K, Heydenrych I (2015) Patient factors influencing dermal filler complications: prevention, assessment, and treatment. Clin Cosmet Investig Dermatol 8:205–214
3. Ferneini EM, Ferneini AM (2016) An overview of vascular adverse events associated with facial soft tissue fillers: recognition, prevention, and treatment. J Oral Maxillofac Surg 74(8):1630–1636
4. Chiang YZ, Pierone G, Al-Niaimi F (2016) Dermal fillers: pathophysiology, prevention and treatment of complications. J Eur Acad Dermatol Venereol. https://doi.org/10.1111/jdv.13977
5. Sundaram H, Cassuto D (2013) Biophysical characteristics of hyaluronic acid soft-tissue fillers and their relevance to aesthetic applications. Plast Reconstr Surg 132(4 Suppl 2):5S–21S
6. Funt D, Pavicic T (2015) Dermal fillers in aesthetics: an overview of adverse events and treatment approaches. Plast Surg Nurs 35:13–32
7. Wagner RD, Fakhro A, Cox JA, Izaddoost SA (2016) Etiology, prevention, and management of infectious complications of dermal fillers. Semin Plast Surg 30(2):83–86
8. Rohrich RJ, Nguyen AT, Kenkel JM (2009) Lexicon for soft tissue implants. Dermatol Surg 35(Suppl 2):1605–1611
9. Dumitraşcu DI, Georgescu AV (2013) The management of biofilm formation after hyaluronic acid gel filler injections: a review. Clujul Med 86(3):192–195
10. Sorensen EP, Urman C (2015) Cosmetic complications: rare and serious events following botulinum toxin and soft tissue filler administration. J Drugs Dermatol 14(5):486–491
11. Hwang CJ (2016) Periorbital injectables: understanding and avoiding complications. J Cutan Aesthet Surg 9(2):73–79
12. Vanaman M, Fabi SG, Carruthers J (2016) Complications in the Cosmetic dermatology patient: a review and our experience (part 1). Dermatol Surg 42(1):1–11
13. Vanaman M, Fabi SG, Carruthers J (2016) Complications in the cosmetic dermatology patient: a review and our experience (part 2). Dermatol Surg 42(1):12–20
14. Gladstone HB, Cohen JL (2007) Adverse effects when injecting facial fillers. Semin Cutan Med Surg 26(1):34–39
15. Shah NS, Lazarus MC, Bugdodel R et al (2002) The effects of topical vitamin K on bruising after laser treatment. J Am Acad Dermatol 47(2):241–244
16. Fitzgerald R, Bertucci V, Sykes JM, Duplechain JK (2016) Adverse reactions to injectable fillers. Facial Plast Surg 32(5):532–555
17. Signorini M, Liew S, Sundaram H, De Boulle KL, Goodman GJ, Monheit G et al (2016) Global aesthetics consensus group. Global aesthetics consensus: avoidance and management of complications from hyaluronic acid fillers-evidence- and opinion-based review and consensus recommendations. Plast Reconstr Surg 137(6):961e–971e
18. Bacci C, Maglione M, Favero L, Perini A, Di Lenarda R, Berengo M et al (2010) Management of dental extraction in patients undergoing anticoagulant treatment. Results from a large, multicentre, prospective, case-control study. Thromb Haemost 104(5):972–975
19. Bacci C, Berengo M, Favero L, Zanon E (2011) Safety of dental implant surgery in patients undergoing anticoagulation therapy: a prospective case-control study. Clin Oral Implants Res 22(2):151–156
20. Jimson S, Amaldhas J, Jimson S, Kannan I, Parthiban J (2015) Assessment of bleeding during minor oral surgical procedures and extraction in patients on anticoagulant therapy. J Pharm Bioallied Sci 7(Suppl 1):S134–S137
21. Eichhorn W, Burkert J, Vorwig O, Blessmann M, Cachovan G, Zeuch J et al (2012) Bleeding incidence after oral surgery with continued oral anticoagulation. Clin Oral Investig 16(5):1371–1376
22. Iwabuchi H, Imai Y, Asanami S, Shirakawa M, Yamane GY, Ogiuchi H et al (2014) Evaluation of postextraction bleeding incidence to compare patients receiving and not receiving warfarin therapy: a cross-sectional, multicentre, observational study. BMJ Open 4(12):e005777
23. Shi Q, Xu J, Zhang T, Zhang B, Liu H (2017) Post-operative bleeding risk in dental surgery for patients on oral anticoagulant therapy: a meta-analysis of observational studies. Front Pharmacol 8:58
24. Urdiales-Gálvez F, Delgado NE, Figueiredo V, Lajo-Plaza JV, Mira M, Ortíz-Martí F et al (2017) Preventing the complications associated with the use of dermal fillers in facial aesthetic procedures: an expert group consensus report. Aesthetic Plast Surg

25. Perry DJ, Noakes TJ, Helliwell PS, British Dental Society (2007) Guidelines for the management of patients on oral anticoagulants requiring dental surgery. Br Dent J 203(7):389–393
26. Leonhardt JM, Lawrence N, Narins RS (2005) Angioedema acute hypersensitivity reaction to injectable hyaluronic acid. Dermatol Surg 31(5):577–579
27. Van Dyke S, Hays GP, Caglia AE, Caglia M (2010) Severe acute local reactions to a hyaluronic acid-derived dermal filler. J Clin Aesthet Dermatol 3(5):32–35
28. Geisler D, Shumer S, Elson ML (2007) Delayed hypersensitivity reaction to Restylane®. Cosmet Dermatol 20(12):784–786
29. Cohen JL, Bhatia AC (2009) The role of topical vitamin K oxide gel in the resolution of postprocedural purpura. J Drugs Dermatol 8(11):1020–1024
30. Christensen LH (2009) Host tissue interaction, fate, and risks of degradable and non-degradable gel fillers. Dermatol Surg 35:1612–1619
31. Glass GE, Tzafetta K (2014) Optimising treatment of Bell's Palsy in primary care: the need for early appropriate referral. Br J Gen Pract 64(629):e807–e809
32. Sclafani AP, Fagien S (2009) Treatment of injectable soft tissue filler complications. Dermatol Surg 35:1672–1680
33. Goodman GJ, Roberts S, Callan P (2016) Experience and management of intravascular injection with facial fillers: results of a multinational survey of experienced injectors. Aesthetic Plast Surg 40(4):549–555
34. Grunebaum LD, Bogdan Allemann I, Dayan S, Mandy S, Baumann L (2009) The risk of alar necrosis associated with dermal filler injection. Dermatol Surg 35(Suppl 2):1635–1640
35. Kwon SG, Hong JW, Roh TS, Kim YS, Rah DK, Kim SS (2013) Ischemic oculomotor nerve palsy and skin necrosis caused by vascular embolization after hyaluronic Acid filler injection: a case report. Ann Plast Surg 71(4):333–334
36. Kim SN, Byun DS, Park JH, Han SW, Baik JS, Kim JY et al (2014) Panophthalmoplegia and vision loss after cosmetic nasal dorsum injection. J Clin Neurosci 21(4):678–680
37. Rzany B, DeLorenzi C (2015) Understanding, avoiding, and managing severe filler complications. Plast Reconstr Surg 136(5 Suppl):196S–203S
38. Cohen JL, Biesman BS, Dayan SH, DeLorenzi C, Lambros VS, Nestor MS et al (2015) Treatment of hyaluronic acid filler-induced impending necrosis with hyaluronidase: consensus recommendations. Aesthet Surg J 35(7):844–849
39. Bailey SH, Cohen JL, Kenkel JM (2011) Etiology, prevention and treatment of dermal filler complications. Aesthetic Surg J 31:110–121
40. Kleydman K, Cohen JL, Marmur E (2012) Nitroglycerin: a review of its use in the treatment of vascular occlusion after soft tissue augmentation. Dermatol Surg 38:1889–1897
41. Park SW, Woos SJ, Park KH, Huth JW, Jung C, Kwon OK (2012) Iatrogenic retinal artery occlusion caused by cosmetic facial filler inyections. Am J Ophthalmol 154(4):653–662
42. Beleznay K, Carruthers JD, Humphrey S, Jones D (2015) Avoiding and treating blindness from fillers: a review of the world literature. Dermatol Surg 41(10):1097–1117
43. Loh KT, Chua JJ, Lee HM, Lim JT, Chuah G, Yim B, Puah BK (2016) Prevention and management of vision loss relating to facial filler injections. Singap Med J 57(8):438–443
44. Carruthers JD, Fagien S, Rohrich RJ, Weinkle S, Carruthers A (2014) Blindness caused by cosmetic filler injection: a review of cause and therapy. Plast Reconstr Surg 134(6):1197–1201
45. Hayreh SS, Zimmerman MB (2005) Central retinal artery occlusion: visual outcome. Am J Ophthalmol 140(3):376–391
46. Arron ST, Neuhaus IM (2007) Persistent delayed-type hypersensitivity reaction to injectable non-animal-stabilized hyaluronic acid. J Cosmet Dermatol 6(3):167–171
47. Cassuto D, Marangoni O, De Santis G, Christensen L (2009) Advanced laser techniques for filler-induced complications. Dermatol Surg 35(Suppl 2):1689–1695
48. Funt DK (2011) Avoiding malar edema during midface/cheek augmentation with dermal fillers. J Clin Aesthet Dermatol 4(12):32–36
49. Taylor SC, Burgess CM, Callender VD (2009) Safety of nonanimal stabilized hyaluronic acid dermal fillers in patients with skin of color: a randomized, evaluator-blinded comparative trial. Dermatol Surg 35(Suppl 2):1653–1660
50. Heath CR, Taylor SC (2011) Fillers in the skin of color population. J Drugs Dermatol 10(5):494–498
51. DeLorenzi C (2013) Complications of injectable fillers, part I. Aesthet Surg J 33(4):561–575
52. Hirsch RJ, Narurkar V, Carruthers J (2006) Management of injected hyaluronic acid induced Tyndall effects. Lasers Surg Med 38(3):202–204
53. Douse-Dean T, Jacob CI (2008) Fast and easy treatment for reduction of the Tyndall effect secondary to cosmetic use of hyaluronic acid. J Drugs Dermatol 7(3):281–283
54. Rousso JJ, Pitman MJ (2010) Enterococcus faecalis complicating dermal filler injection: a case of virulent facial abscesses. Dermatol Surg 36(10):1638–1641
55. Christensen LH (2009) Host tissue interaction, fate, and risks of degradable and nondegradable gel fillers. Dermatol Surg 35(Suppl 2):1612–1619
56. Dayan SH, Arkins JP, Brindise R (2011) Soft tissue fillers and biofilm. Facial Plast Surg 27:23–28
57. Ledon JA, Savas JA, Yang S, Franca K, Camacho I, Nouri K (2013) Inflammatory nodules following soft tissue filler use: a review of causative agents, pathology and treatment options. Am J Clin Dermatol 14:401–411
58. Bjarnsholt T, Tolker-Nielsen T, Givskov M, Janssen M, Christensen LH (2009) Detection of bacteria by fluorescence in situ hybridization in culture-negative soft tissue filler lesions. Dermatol Surg 35(Suppl 2):1620–1624
59. Attila C, Ueda A, Wood TK (2009) 5-Fluorouracil reduces biofilm formation in Escherichia coli K-12 through global regulator AriR as an antivirulence compound. Appl Microbiol Biotechnol 82(3):525–533
60. Tohidnezhad M, Varoga D, Wruck CJ, Podschun R, Sachweh BH, Bornemann J et al (2012) Platelets display potent antimicrobial activity and release human beta-defensin 2. Platelets 23(3):217–223
61. Albeiroti S, Ayasoufi K, Hill DR, Shen B, de la Motte CA (2015) Platelet hyaluronidase-2: an enzyme that translocates to the surface upon activation to function in extracellular matrix degradation. Blood 125(9):1460–1469
62. Różalski MI, Micota B, Sadowska B, Paszkiewicz M, Więckowska-Szakiel M, Różalska B (2013) Antimicrobial/anti-biofilm activity of expired blood platelets and their released products. Postepy Hig Med Dosw (Online) 67:321–325
63. Lemperle G, Gauthier-Hazan N, Wolters M, Eisemann-Klein M, Zimmermann U, Duffy DM (2009) Foreign body granulomas after all injectable dermal fillers: part 1. Possible causes. Plast Reconstr Surg 123(6):1842–1863
64. Lemperle G, Gauthier-Hazan N (2009) Foreign body granulomas after all injectable dermal fillers: part 2. Treatment options. Plast Reconstr Surg 123(6):1864–1873
65. Hirsch RJ, Cohen JL, Carruthers JD (2007) Successful management of an unusual presentation of impending necrosis following a hyaluronic acid injection embolus and a proposed algorithm for management with hyaluronidase. Dermatol Surg 33(3):357–360
66. Bachmann F, Erdmann R, Hartmann V, Wiest L, Rzany B (2009) The spectrum of adverse reactions after treatment with injectable fillers in the glabellar region: results from the

Injectable Filler Safety Study. Dermatol Surg 35(Suppl 2):1629–1634
67. Schanz S (2002) Arterial embolization caused by injection of hyaluronic acid (Restylane). Br J Dermatol 146:928–929
68. Beer K, Downie J, Beer J (2012) A treatment protocol for vascular occlusion from particulate soft tissue augmentation. J Clin Aesthet Dermatol 5(5):44–47

Colby L. Presley, DO‡
Anthony M. Rossi, MD§
* Department of Internal Medicine, Mount Sinai Hospital, New York, New York
† Department of Dermatology, Duke University, Durham, North Carolina
‡ Division of Dermatology, Lehigh Valley Health Network, Allentown, Pennsylvania
§ Department of Dermatology, Memorial Sloan Kettering Cancer Center, New York, New York

This research was funded, in part, by NIH/NCI Cancer Center Support Grant P30 CA008748.

The authors have indicated no significant interest with commercial supporters.

Trends in Medical Spa Statistics and Patient Safety

In 2023, the medical spa industry in the United States is projected to garner as much as $20 billion in revenue, doubled from just 4 years prior.[1] This net growth occurred even as 84% of medical spa locations temporarily closed their doors because of the global COVID-19 pandemic.[1] By 2025, the annual revenue is expected to increase by another 25%.[1] Anyone can open a clinic by collaborating with a licensed member of the medical community, which may account for 70% of the medical spas lacking any affiliation with a medical practice.[1]

The average annual revenue expected for an individual medical spa is more than $1.5 million as of 2021, with an annual expected growth of >10%.[1] Consequently, this is an immensely profitable industry that has exploded in popularity in the past decade. Since 2010, the number of medical spas nationwide have increased nearly six-fold and currently employ more than 70 thousand people.[1] These clinics offer various services including botulinum toxin, injectable fillers, and laser procedures. However, questions abound regarding the safety of these procedures to the consumer in an industry growing faster than it can be regulated.

As of 2022, 66% of medical spas were owned by a private, single individual; however, only 37% were owned by physicians. Of the physician-owned spas, dermatologists accounted for only 4%, despite being one of the few specialties with postgraduate residency training requirements in cosmetics. 23% of single-owner medical spas were owned by nurse practitioners, doubling from 11% in 2019 (Figure 1).[1]

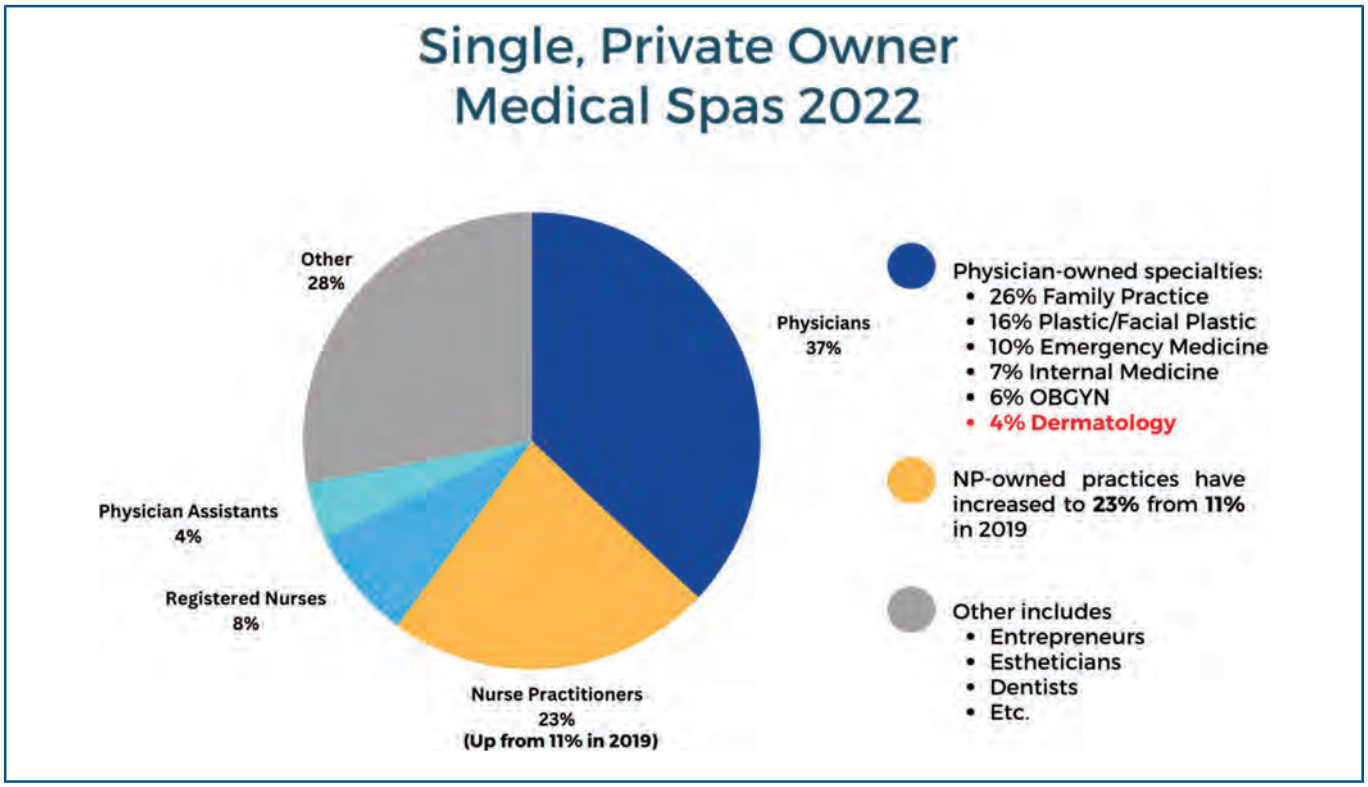


Figure 1. According to the AmSpa State of the Industry Report, 37% of single, private owner medical spas were owned by physicians in 2022. Merely 4% of physician-owned medical spas were owned by dermatologists. Medical spas owned by NPs (nurse practitioners) have more than doubled from 11% to 23% since 2019.

A 2020 survey demonstrated that 70% of surveyed dermatologists in the United States reported seeing at least 1 patient, and as many as 20, with cosmetic complications in the past 2 years. Most of these were attributable to treatments received from medical spas.[2] The most common complications included burn, discoloration, misplacement of product, bruising, and scar. From 2008 to 2011, the number of litigated cases involving a nonphysician performing laser surgery more than doubled. Similarly, from 2008 to 2012, nonphysicians performing laser hair removal represented approximately 85.7% of lawsuits despite performing only one-third of laser hair removal procedures in 2012.[3] These authors concluded that there is inherent risk in acquiring cosmetic services through nonphysicians.[3] By contrast, dermatologists accounted for laser complication rates of 0.24%.[4]

Most surveyed dermatologists believe that medical spas jeopardize patient safety and warrant increased regulation by governing bodies.[2] However, federal and state governments have not tightly regulated the medical spa industry. Given the variable geographic distribution of medical spas in the United States, meaningful legislation may have to occur at the state level.[5] Ideally, regulations would acknowledge that most cosmetic dermatologic procedures are safe when performed by board-certified dermatologists.[4] This calls for dermatologists to educate patients and lawmakers on the potential complications of seeking cosmetic procedures by inadequately trained or inadequately supervised practitioners at medical spas.

References

1. 2022 Medical Spa State of the Industry Report. *American Med Spa Association in Partnership with Gordian Solutions Group®*; 2022.
2. Wang JV, Albornoz CA, Goldbach H, Mesinkovska N, et al. Experiences with medical spas and associated complications: a survey of aesthetic practitioners. *Dermatol Surg* 2020;46:1543–8.
3. Jalian HR, Jalian CA, Avram MM. Increased risk of litigation associated with laser surgery by nonphysician operators. *JAMA Dermatol* 2014;150:407–11.
4. Alam M, Kakar R, Nodzenski M, Ibrahim O, et al. Multicenter prospective cohort study of the incidence of adverse events associated with cosmetic dermatologic procedures: lasers, energy devices, and injectable neurotoxins and fillers. *JAMA Dermatol* 2015;151:271–7.
5. Handley R. The medi-spa: a current cosmetic dermatology public safety concern. *Internet J Acad Phys Assist* 2008;7:1–7.

Justin Eichinger, MS*
Jarett Casale, DO†
Phuong Daniels, DO, DPT†
Ashley Rice, DO, FAAD†
**University of Louisville School of Medicine, Louisville, Kentucky*
†Campbell University at Sampson Regional Medical Center, Clinton, North Carolina

The authors have indicated no significant interest with commercial supporters.

Original Article

Who Is Holding the Syringe? A Survey of Truth in Advertising Among Medical Spas

Sara Hogan, MD, FAAD,* Emily Wood, MD, FAAD,† and Vineet Mishra, MD, FAAD, FACMS‡

BACKGROUND The degree of supervision and level of expertise required for performing cosmetic procedures differs significantly from state to state. Medical spas providing cosmetic procedures have seen exponential growth since 2020.

OBJECTIVE To provide a representative sample of the medical spa industry in the Unites States regarding the expertise among providers performing cosmetic procedures and the degree of oversight at medical spas offering these procedures.

MATERIALS AND METHOD Descriptive study based on a standardized telephone interview performed by a secret shopper in Chicago and surrounding suburbs. Data were then extracted and analyzed.

RESULTS Of 127 medical spas reviewed, a supervising physician was not on-site at 81.1% of the facilities. Patients were informed of this at 64.6% of the surveyed medical spas.

CONCLUSION There is considerable variation in the oversight and in the training among those performing cosmetic procedures at surveyed medical spas. As cosmetic procedures become increasingly popular among the public, further regulation of medical spas is warranted to protect patient safety.

Medical spas, or medi-spas, integrate aesthetic medical services with traditional spa services under the supervision of a licensed physician. In the United States, medical spas are a $15 billion industry, employing more than 70,000 personnel.[1] The current growth of medical spas in this country is exponential. In 2021, the American Medical Spa Association (AmSPA) reports 7,430 spas in the United States, which increased to 8,841 spas in 2022. This corresponds with growth in average revenue of $1,722,551 per spa in 2021 to $1,982,896 per spa in 2022.[1] The increase in number of facilities and revenue reflects data showing that since 2015, consumer interest (e.g. Google search inquiries) in medical spas and cosmetic procedures has grown.[2] Medical spas are also likely more accessible to consumers given decreased wait times compared with physician offices.[3] Growing interest, greater accessibility, and rising profitability, therefore, suggest that many cosmetic patients are not having their procedures performed in physician offices, but rather medical spas.

*From the *Department of Dermatology, The George Washington University, Washington, DC; †Westlake Dermatology, Austin, Texas; ‡Department of Dermatology, University of California, San Diego San Diego, California*

This paper was funded by The American Society for Dermatologic Surgery.

The authors have indicated no significant interest with commercial supporters.

Preliminary results of this study were presented October 7, 2022 as a Future Leaders Network presentation at the American Society for Dermatologic Surgery Annual Meeting in Chicago, IL.

Address correspondence and reprint requests to: Sara Hogan, MD, FAAD, Luxe Dermatology and Aesthetic Center, 8200 Greensboro Drive, Suite 801, Mclean, VA 22102, or sara.hogan@gmail.com

Dermatol Surg 2023;00:1–5
http://dx.doi.org/10.1097/DSS.0000000000003929

According to AmSPA, 63% of member medical spas have non-Doctor of Medicine (MD) ownership.[1] Among those medical spas owned by physicians, 80% are of noncore aesthetic specialties, meaning a medical specialty other than dermatology, plastic surgery, otorhinolaryngology, or ophthalmology. Of member medical spa directors, 69% are of a noncore specialty.[1] Recent studies highlight a trend of increased delegation of cosmetic procedures by both dermatologists and nondermatologists to nonphysician providers.[4–6] Nonphysician providers (e.g., physician assistants, nurse practitioners, and registered nurses) lack equivalent or standardized procedural training compared with physicians.

The delegation of cosmetic procedures can place patients at increased risk for adverse events. This is specifically documented for laser surgery, for which state-to-state regulations vary considerably and for which an increased risk of medical professional liability claims is observed among nonphysician providers.[7,8] At medical spas, this relative higher incidence of complications for cosmetic procedures is likely due to improper training, improper technique, and/or improper cosmetic device settings.[9]

Patients may not be aware of the credentials or the oversight of the provider performing their cosmetic procedure or the potential risks to their health. The aim of this study was to elucidate who performs cosmetic procedures, provides medical supervision, and follows safety protocols at medical spas, and the extent to which medical spa staff are transparent regarding this information to cosmetic patients.

Chicago and its surrounding areas were selected as the study site. In a 2020 study, Chicago was identified as the US city with the third greatest number of aesthetic physicians (122 or 0.45 per 10,000 persons) and the fifth highest

number of medical spas (166 or 0.61 medical spas per 10,000 persons).[10] Chicago has a high ratio of medical spas to aesthetic physicians (1.36), suggesting that a considerable number of cosmetic procedures are being performed by nonphysician providers.[10]

Methods

In April 2022, the authors queried Google, Facebook, and Yelp websites with the search terms "medical spa," "medi-spa," "medspa," and "Chicago." The queries yielded 138 medical spas in the Chicagoland area. Websites were reviewed, and contact information, available services, and medical director information, if available, were recorded. A script regarding inquiry for new patient services was developed by the authors. Secret shoppers then contacted the 138 medical spas through telephone and recorded responses from staff. Information was collected, extracted into a usable data set, and analyzed using R (R Core Team, 2013). This study did not involve experimentation on human subjects and is exempt from Institutional Review Board review. The authors were responsible for the database queries, review, and analysis.

Results

Of the 138 identified medical spas, 11 spas could not be reached or, when contacted, were not a medical spa (e.g., solo aesthetician practice), bringing the total to 127. The most common cosmetic procedures provided at queried medical spas were facials and laser hair removal (both 85%), followed by neuromodulator injections (83.5%) and soft-tissue dermal filler injections (82.7%) (Figure 1).

Aestheticians and registered nurses/licensed practical nurses perform cosmetic consultations at most of the medical spas in this study (64.6% and 51.2%, respectively). A supervising physician is available to conduct an in-person cosmetic consultation at 41.7% of surveyed medical spas. A patient's medical history is reviewed by a supervising physician at 40.9% of those medical spas, although it is not clear how consistently this is performed. At most of the surveyed medical spas, cosmetic procedures are performed by aestheticians and nurses, 66.9% and 52.8%, respectively (Figure 2). A physician supervises or personally performs cosmetic procedures on-site at approximately half (53.5%) of the medical spas in this study (Figure 3).

Eighty-four percent of medical spas in this study endorsed having a medical director or supervising Doctor of Medicine (MD)/Doctor of Osteopathic Medicine (DO) physician. Among these medical directors and supervising MDs/DOs, only 69.3% are reported to be board-certified in a medical specialty. The top reported medical specialties of medical spa directors are Plastic and Reconstructive Surgery (19). (Table 1).

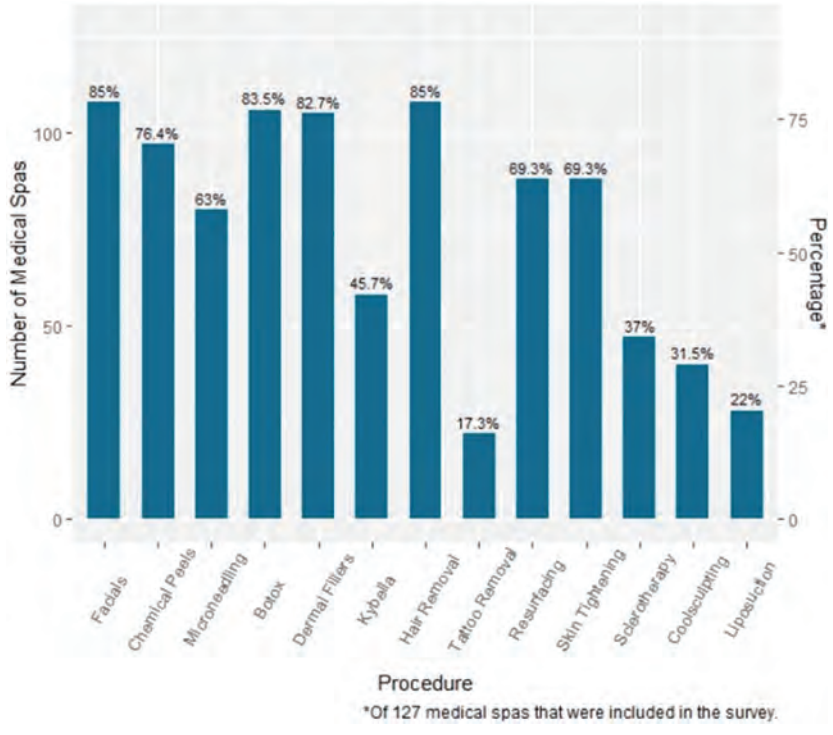


Figure 1. Cosmetic procedures offered at study medical spas.

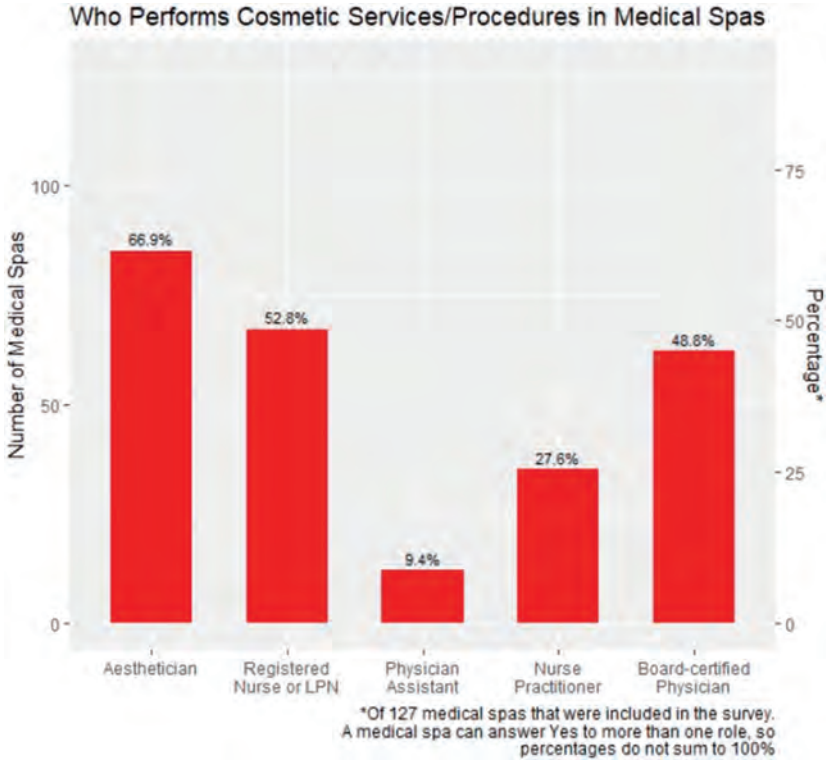


Figure 2. Medical spa cosmetic procedure provider by training.

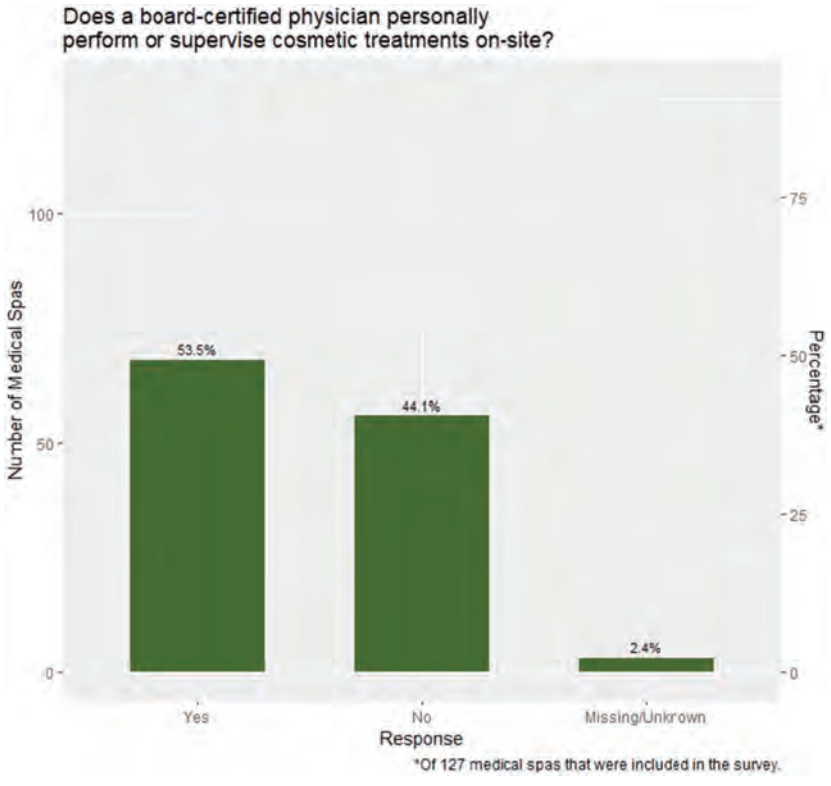


Figure 3. Board-certified physicians performing cosmetic treatments at study medical spas.

TABLE 1. Study Medical Spa Directors or Supervising Physicians by Medical Specialty

Reported Medical Specialty	Count
Aesthetic medicine	1
Anesthesiology	3
Cosmetic surgery	9
Dermatology	5
Emergency medicine	3
Family medicine	8
Gastroenterology	1
Hair restoration surgery	1
Internal medicine	12
Internal medicine and dermatology	1
Obstetrics and gynecology	5
Ophthalmology	1
Optometry	1
Oral and maxillofacial surgery	1
Pediatrics	3
Pediatric surgery	1
Plastic and reconstructive surgery	19
Plastic surgery nursing certification	1
Psychiatry	1
Radiology	1
Unknown	6
Vascular medicine	1

A medical director or supervising MD/DO is always on-site at 16.5% of reporting medical spas. If not located on-site, the medical director or supervising MD/DO is located at their primary practice (e.g., office or hospital) for 62.1% of reporting medical spas and in the same city as 23.3% of surveyed medical spas (Figure 4). Sixty-five percent of queried medical spas state that they inform patients that the medical director or supervising MD/DO is not on-site.

In the event of a complication or unwanted side effect from a cosmetic procedure, 70.1% of surveyed medical spas notify a medical director/supervising MD or DO. When asked about protocols for the management of cosmetic complications, responses vary. The most common answer was that patients are given an after-hours number at the time of their cosmetic procedure and that a nurse staff member monitors this phone line and performs triage.

Discussion

This study contributes to a growing amount of evidence demonstrating that most cosmetic procedures offered at medical spas are performed by nonphysician providers. Oversight at medical spas differs greatly and is inconsistent across the United States. State medical boards determine guidelines regarding what constitutes a medical procedure, the delegation of such procedures, on-site versus off-site physician supervision, and the staffing ratio of supervising physicians to nonphysicians. For example, a supervising physician in California is not required to be present during procedures at a medical spa but must be "immediately reachable" by phone or e-mail at all times. While in Florida, a medical spa should be within 25 miles of a supervising physician's primary place of practice, and the distance between any of the physician's offices may not exceed 75 miles.

The combination of nonphysician administration of cosmetic procedures and inconsistency in medical supervision places patients of medical spas at risk for procedural complications. In one study evaluating the litigation of cosmetic procedures, 64% of litigated cases were performed outside of a traditional medical setting, such as medical spa.[8] A significant number of the litigated cases involved allegations of lack of supervision or proper training of nonphysician providers.[8]

Among those medical spas the authors surveyed, a supervising physician was not on-site at 81.1% of the facilities. Staff informed patients of this information at 64.6% of the medical spas. This means that many patients are not aware that medical spa staff are performing cosmetic procedures without the direct supervision of a medical director or supervising physician. Patients are also likely unaware that, should a cosmetic procedural complication occur, a medical director or supervising physician would not readily be available for medical evaluation and management.

One limitation of this study is that the authors did not determine which cosmetic procedures are performed by which medical spa service provider (e.g., laser resurfacing performed by a nurses vs a physician). Another limitation is that with the geography of the study being limited to Chicago and surrounding areas, nationwide conclusions are difficult to determine. Further studies are needed to better understand the true extent of this phenomenon.

Conclusion

There is significant variation in the supervision and level of training among those performing cosmetic procedures at medical spas. The cosmetic patient is often unaware of the vast differences in education and supervision among medical spa providers. Improved regulation of cosmetic procedures performed at medical spas, and guidelines regarding on-site versus off-site supervision and the staffing ratio of supervising physicians to nonphysicians, is needed to protect patient safety.

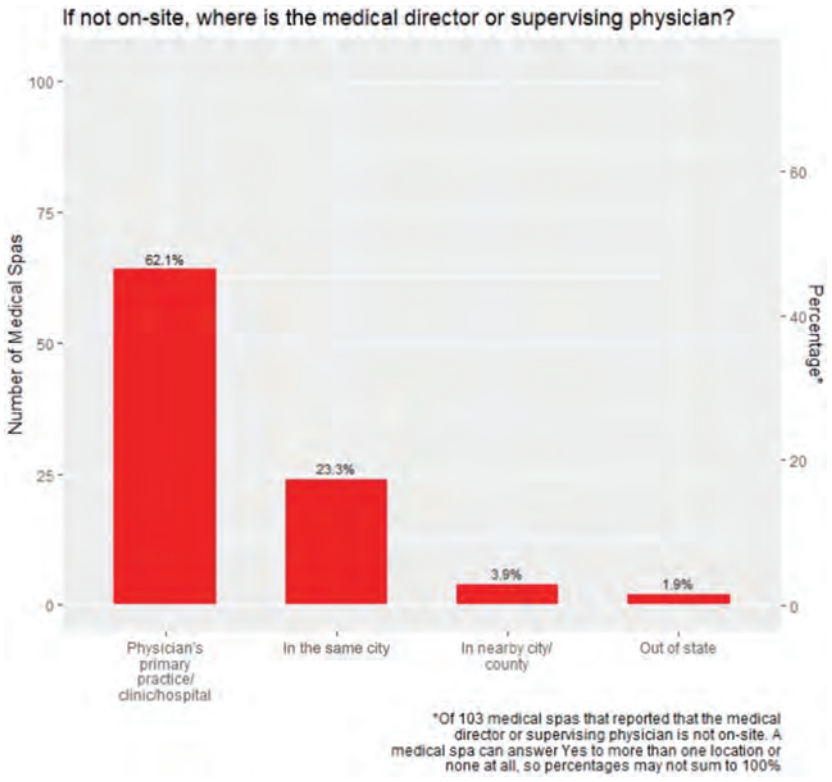


Figure 4. Physical location of study medical spa directors or supervising physicians.

Acknowledgments

Seth Pixton had full access to all the data in the study and facilitated with data analysis.

References

1. American Med Spa Association. *Medical Spa State of the Industry: Executive Summary*. Chicago, IL: AmSPA; 2022. Available from: https://americanmedspa.org/resources/med-spa-statistics. Accessed February 15, 2023.
2. Wang JV, Albornoz CA, Zachary CB, Saedi N. Evolution of search trends for medical spas and cosmetic dermatologists: a 2009 to 2019 national comparison. *Dermatol Surg* 2021;47:872–4.
3. Wang JV, Shah S, Albornoz CA, Rohrer T, et al. Medical spa or physician practice: the national impact of patient wait times in aesthetics. *Dermatol Surg* 2021;47:887–9.
4. Austin MB, Srivastava D, Bernstein IH, Dover JS. A survey comparing delegation of cosmetic procedures between dermatologists and nondermatologists. *Dermatol Surg* 2015;41:827–32.
5. Brody HJ, Geronemus RG, Farris PK. Beauty versus medicine: the nonphysician practice of dermatologic surgery. *Dermatol Surg* 2003;29:319–24.
6. Gibson JF, Srivastava D, Nijhawan RI. Medical oversight and scope of practice of medical spas (med-spas). *Dermatol Surg* 2019;45:581–7.
7. DiGiorgio CM, Avram MM. Laws, and regulations of laser operation in the United States. *Lasers Surg Med* 2018;50:272–9.
8. Jalian HR, Jalian CA, Avram M. Increased risk of litigation associated with laser surgery by nonphysician operators. *Jama Dermatol* 2014;150:407–11.
9. Wang JV, Albornoz CA, Goldbach H, Mesinkovska N, et al. Experiences with medical spas and associated complications: a survey of aesthetic practitioners. *Dermatol Surg* 2020;46:1543–8.
10. Wang JV, Albornoz CA, Noell C, Friedman PM, et al. Skewed distribution of medical spas and aesthetic physician practices: a cross-sectional market analysis. *Dermatol Surg* 2021;47:397–9.

ATTACHMENT E

December 2, 2024

William M. Perkins
Executive Director
Alabama Board of Medical Examiners
848 Washington Avenue
Montgomery, AL 36104

RE: Oppose Botulinum Toxin A and Dermal Fillers for Cosmetic Purposes Scope of Practice Expansion

Dear Mr. Perkins:

On behalf of the American Academy of Dermatology Association and the American Society for Dermatologic Surgery Association representing more than 17,000 dermatologists nationwide, we are writing to share our concerns with proposals that request the Alabama Board of Medical Examiners to authorize certified registered nurse practitioners (CRNP), physician assistants (PA) and registered nurses (RN) to administer botulinum toxin A and dermal fillers for cosmetic purposes.

Procedures by any means, methods, devices or instruments that can alter or cause biologic change or damage the skin and subcutaneous tissue constitute the practice of medicine and surgery. This includes the use of foreign or natural substances by injection or insertion. [i,ii] Our organizations believe that medical procedures using a Food and Drug Administration (FDA)-regulated device, such as those that can alter or cause biologic change or damage, should only be performed by a physician or appropriately trained non-physician personnel under the direct, onsite supervision of an appropriately trained physician.[iii] These proposals jeopardize patient safety and disregard what is considered adequate and appropriate medical education and training. Quality patient care includes evaluating a patient's needs and condition(s), selecting an appropriate course of treatment and providing adequate follow-up care.

With the growing public demand for facial fillers and neuromodulators, providing patients with properly trained, educated, and supervised medical personnel is a safeguard Alabama should have for its citizenry. Fillers and neuromodulators can also be used to treat scars from injury and surgery, as well as from medical conditions; other applications include correcting facial asymmetries resulting from congenital, accidental, or medical conditions. Our utmost concern is to ensure that these products are safely administered by licensed and qualified physicians or under the direct, on-site supervision of a licensed and qualified physician. "As with other cutaneous procedures, it is necessary to receive adequate training before using soft-tissue augmentation agents. Physician injectors should first be made to demonstrate a detailed knowledge of anatomy and possible adverse events (such as sensitivity, infection, and necrosis) through passing an American Board of Medical Specialties (or an ABMS-equivalent Board) examination in one of the CORE aesthetic specialties after residency training in one of these disciplines." [iv]

There are substantial differences in the education of non-physicians and physicians, both in depth of knowledge and length of training. Board certified dermatologists diagnose and treat over 3,000 different diseases and conditions. Dermatologists see patients of all ages – from newborns to the elderly. A board certified

dermatologist undertakes a minimum of 8 years of exhaustive medical education and training (4 years of medical school, 1 year of internship, 3 years (minimum) of dermatology residency), during which they complete 12,000 to 16,000 hours of direct patient care, before they can practice independently. Dermatologists must pass 3 standardized USMLE training exams to become licensed physicians and then pass a comprehensive examination at the conclusion of their residency training to become board certified in dermatology. Dermatologists have focused training in using fillers and neuromodulators involving the skin and adjacent structures, which prepares them to perform medical procedures using fillers and neuromodulators safely and effectively. Included in this training is proper technique, and the management of any adverse events.

In contrast, non-physicians have less clinical experience than a physician obtains in just the first year of a three-year medical residency. CRNPs obtain 500 to 720 hours of direct patient care, and PAs obtain 2,000 hours of clinical rotations after completing a 26-month program. These rotations emphasize primary care in ambulatory clinics, physician offices and acute or long-term care facilities.[v] Unlike physicians, non-physicians are not required to complete a residency program or demonstrate competency in procedures involving skin and soft tissue augmentation with products that can alter or damage living tissue. It is of upmost importance that the physician or non-physician performing procedures with neurotoxins (such as botulinum toxin) or dermal fillers have specific, long-term training (such as a medical residency in dermatology or plastic surgery). The education for non-physicians does not include this type of intense training; additionally, any short-term training program offered by manufacturers of these products does not adequately protect patient safety.

During a 2021 meeting of the FDA's General and Plastic Surgery Committee on Soft-Tissue Fillers, the American Society for Dermatologic Surgery's Task Force on Soft-Tissue Fillers found that knowledge of vascular anatomy is *crucial* for all filler injections. **Intravascular injection is possible at any location on the face, but certain locations carry a higher risk, such as filler embolization; necrosis; visual abnormalities; blindness; and stroke.**[vi] Thus, we are in firm agreement with the FDA's further updated consumer guidance in 2023 that anyone considering a neurotoxin or dermal filler consult with a licensed provider who is experienced in injecting dermal fillers, knowledgeable about fillers, anatomy, managing complications and knows the risks and benefits of treatment.[vii] Furthermore, the American Medical Association (AMA) states that, "Cosmetic medical procedures, such as botulinum toxin injections, dermal filler injections, and laser and intense pulsed light procedures, be considered the practice of medicine."[viii]

To best protect the citizens of Alabama from adverse events and ensure quality patient care, **we respectfully ask that the Alabama Board of Medical Examiners oppose the request to expand the scope of practice of CRNPs, PAs and RNs to include the administration of botulinum toxin A and dermal fillers for cosmetic purposes.** Thank you for your strong consideration on this matter. Should you have any questions regarding this critical patient safety issue, please do not hesitate to contact Kristin Hellquist, Chief Advocacy Officer at the American Society for Dermatologic Surgery Association, at khellquist@asds.net.

Sincerely,

American Academy of Dermatology Association
American Society for Dermatologic Surgery Association

[i] ASDSA *Position Statement on the Practice of Medicine*. https://www.asds.net/Portals/0/PDF/asdsa/asdsa-position-statement-definition-of-the-practice-of-medicine.pdf
[ii] AADA *Position Statement on Medical Spa Standards of Practice*. https://www.aad.org/Forms/Policies/Uploads/PS/PS-Medical%20Spa%20Standards%20of%20Practice.pdf
[iii] ASDSA *Position Statement on Delegation*. https://www.asds.net/Portals/0/PDF/asdsa/asdsa-position-statement-delegation.pdf
[iv] Gladstone H, Cohen J. Adverse Effects When Injecting Facial Fillers. Semin Cutan Med Surg. 2007 Mar;26(1):34-9.
[v] How are PAs Educated and Trained? https://www.aapa.org/what-is-a-pa/#tabs-2-how-are-pas-educated-and-trained

ATTACHMENT E

[vi] Jones D, Fitzgerald R, Cox S, Butterwick K, et al. Preventing and Treating Adverse Events of Injectable Fillers: Evidence-Based Recommendations From the American Society for Dermatologic Surgery Multidisciplinary Task Force. Dermatol Surg 2021;47:214-26.
[vii] Filling in Wrinkles Safely. Accessed Aug. 6, 2024. Retrieved from https://www.fda.gov/ForConsumers/ConsumerUpdates/ucm049349.htm
[viii] Addressing Safety and Regulation in Medical Spas. Retrieved Aug. 6, 2024. https://policysearch.ama-assn.org/policyfinder/detail/dermal%20fillers?uri=%2FAMADoc%2Fdirectives.xml-0-1174.xml

ATTACHMENT F

MEDICATION GUIDE
BOTOX®
BOTOX® Cosmetic
(Boe-tox)
(onabotulinumtoxinA)
for Injection

What is the most important information I should know about BOTOX and BOTOX Cosmetic?

BOTOX and BOTOX Cosmetic may cause serious side effects that can be life threatening, including:

- **Problems breathing or swallowing**
- **Spread of toxin effects**

These problems can happen hours, days, to weeks after an injection of BOTOX or BOTOX Cosmetic. Call your doctor or get medical help right away if you have any of these problems after treatment with BOTOX or BOTOX Cosmetic:

1. Problems swallowing, speaking, or breathing. These problems can happen hours, days, to weeks after an injection of BOTOX or BOTOX Cosmetic usually because the muscles that you use to breathe and swallow can become weak after the injection. Death can happen as a complication if you have severe problems with swallowing or breathing after treatment with **BOTOX** or **BOTOX Cosmetic**.

- People with certain breathing problems may need to use muscles in their neck to help them breathe. These people may be at greater risk for serious breathing problems with **BOTOX** or **BOTOX Cosmetic**.
- Swallowing problems may last for several months. People who cannot swallow well may need a feeding tube to receive food and water. If swallowing problems are severe, food or liquids may go into your lungs. People who already have swallowing or breathing problems before receiving **BOTOX** or **BOTOX Cosmetic** have the highest risk of getting these problems.

2. Spread of toxin effects. In some cases, the effect of botulinum toxin may affect areas of the body away from the injection site and cause symptoms of a serious condition called botulism. The symptoms of botulism include:

- loss of strength and muscle weakness all over the body
- double vision
- blurred vision and drooping eyelids
- hoarseness or change or loss of voice (dysphonia)
- trouble saying words clearly (dysarthria)
- loss of bladder control
- trouble breathing
- trouble swallowing

These symptoms can happen hours, days, to weeks after you receive an injection of **BOTOX** or **BOTOX Cosmetic**.

These problems could make it unsafe for you to drive a car or do other dangerous activities. See "What should I avoid while receiving **BOTOX** or **BOTOX Cosmetic**?"

There has not been a confirmed serious case of spread of toxin effect away from the injection site when **BOTOX** has been used at the recommended dose to treat chronic migraine, severe underarm sweating, blepharospasm, or strabismus, or when **BOTOX Cosmetic** has been used at the recommended dose to treat frown lines and/or crow's feet lines.

ATTACHMENT F

What are BOTOX and BOTOX Cosmetic?

BOTOX is a prescription medicine that is injected into muscles and used:

- to treat overactive bladder symptoms such as a strong need to urinate with leaking or wetting accidents (urge urinary incontinence), a strong need to urinate right away (urgency), and urinating often (frequency) in adults when another type of medicine (anticholinergic) does not work well enough or cannot be taken.
- to treat leakage of urine (incontinence) in adults with overactive bladder due to neurologic disease when another type of medicine (anticholinergic) does not work well enough or cannot be taken.
- to prevent headaches in adults with chronic migraine who have 15 or more days each month with headache lasting 4 or more hours each day.
- to treat increased muscle stiffness in elbow, wrist, and finger muscles in adults with upper limb spasticity.
- to treat increased muscle stiffness in ankle and toe muscles in adults with lower limb spasticity.
- to treat the abnormal head position and neck pain that happens with cervical dystonia (CD) in adults.
- to treat certain types of eye muscle problems (strabismus) or abnormal spasm of the eyelids (blepharospasm) in people 12 years and older.

BOTOX is also injected into the skin to treat the symptoms of severe underarm sweating (severe primary axillary hyperhidrosis) when medicines used on the skin (topical) do not work well enough.

BOTOX Cosmetic is a prescription medicine that is injected into muscles and used to improve the look of moderate to severe frown lines between the eyebrows (glabellar lines) in adults for a short period of time (temporary).

BOTOX Cosmetic is a prescription medicine that is injected into the area around the side of the eyes to improve the look of crow's feet lines in adults for a short period of time (temporary).

You may receive treatment for frown lines and crow's feet lines at the same time.

It is not known whether **BOTOX** is safe or effective in people younger than:

- 18 years of age for treatment of urinary incontinence
- 18 years of age for treatment of chronic migraine
- 18 years of age for treatment of spasticity
- 16 years of age for treatment of cervical dystonia
- 18 years of age for treatment of hyperhidrosis
- 12 years of age for treatment of strabismus or blepharospasm

BOTOX Cosmetic is not recommended for use in children younger than 18 years of age.

It is not known whether **BOTOX** and **BOTOX Cosmetic** are safe or effective to prevent headaches in people with migraine who have 14 or fewer headache days each month (episodic migraine).

It is not known whether **BOTOX** and **BOTOX Cosmetic** are safe or effective for other types of muscle spasms or for severe sweating anywhere other than your armpits.

Who should not take BOTOX or BOTOX Cosmetic?

Do not take **BOTOX** or **BOTOX Cosmetic** if you:

- are allergic to any of the ingredients in **BOTOX** or **BOTOX Cosmetic**. See the end of this Medication Guide for a list of ingredients in **BOTOX** and **BOTOX Cosmetic**.
- had an allergic reaction to any other botulinum toxin product such as *Myobloc®*, *Dysport®*, *or Xeomin®*
- have a skin infection at the planned injection site
- are being treated for urinary incontinence and have a urinary tract infection (UTI)
- are being treated for urinary incontinence and find that you cannot empty your bladder on your own (only applies to people who are not routinely catheterizing)

What should I tell my doctor before taking BOTOX or BOTOX Cosmetic?

Tell your doctor about all your medical conditions, including if you:

- have a disease that affects your muscles and nerves (such as amyotrophic lateral sclerosis [ALS or Lou Gehrig's disease], myasthenia gravis or Lambert-Eaton syndrome). See "What is the most

important information I should know about **BOTOX** and **BOTOX Cosmetic**?"

- have allergies to any botulinum toxin product
- had any side effect from any botulinum toxin product in the past
- have or have had a breathing problem, such as asthma or emphysema
- have or have had swallowing problems
- have or have had bleeding problems
- have plans to have surgery
- had surgery on your face
- have weakness of your forehead muscles, such as trouble raising your eyebrows
- have drooping eyelids
- have any other change in the way your face normally looks
- have symptoms of a urinary tract infection (UTI) and are being treated for urinary incontinence. Symptoms of a urinary tract infection may include pain or burning with urination, frequent urination, or fever.
- have problems emptying your bladder on your own and are being treated for urinary incontinence
- are pregnant or plan to become pregnant. It is not known if **BOTOX** or **BOTOX Cosmetic** can harm your unborn baby.
- are breast-feeding or plan to breastfeed. It is not known if **BOTOX** or **BOTOX Cosmetic** passes into breast milk.

Tell your doctor about all the medicines you take, including prescription and nonprescription medicines, vitamins and herbal products. Using **BOTOX** or **BOTOX Cosmetic** with certain other medicines may cause serious side effects. **Do not start any new medicines until you have told your doctor that you have received BOTOX or BOTOX Cosmetic in the past.**

Especially tell your doctor if you:

- have received any other botulinum toxin product in the last four months
- have received injections of botulinum toxin, such as *Myobloc*® (rimabotulinumtoxinB), *Dysport*® (abobotulinumtoxinA), *or Xeomin*® (incobotulinumtoxinA) in the past. Be sure your doctor knows exactly which product you received.
- have recently received an antibiotic by injection
- take muscle relaxants
- take an allergy or cold medicine
- take a sleep medicine
- take anti-platelets (aspirin-like products) and/or anti-coagulants (blood thinners)

Ask your doctor if you are not sure if your medicine is one that is listed above.

Know the medicines you take. Keep a list of your medicines with you to show your doctor and pharmacist each time you get a new medicine.

How should I take BOTOX or BOTOX Cosmetic?

- **BOTOX** or **BOTOX Cosmetic** is an injection that your doctor will give you.
- **BOTOX** is injected into your affected muscles, skin, or bladder.
- **BOTOX Cosmetic** is injected into your affected muscles.
- Your doctor may change your dose of **BOTOX** or **BOTOX Cosmetic**, until you and your doctor find the best dose for you.
- **Your doctor will tell you how often you will receive your dose of BOTOX or BOTOX Cosmetic injections.**

What should I avoid while taking BOTOX or BOTOX Cosmetic?

BOTOX and **BOTOX Cosmetic** may cause loss of strength or general muscle weakness, vision problems, or dizziness within hours to weeks of taking **BOTOX** or **BOTOX Cosmetic**. **If this happens, do not drive a car, operate machinery, or do other dangerous activities.** See "What is the most

important information I should know about **BOTOX** and **BOTOX Cosmetic**?"

What are the possible side effects of BOTOX and BOTOX Cosmetic?

BOTOX and BOTOX Cosmetic can cause serious side effects. See "What is the most important information I should know about **BOTOX** and **BOTOX Cosmetic**?"

Other side effects of BOTOX and BOTOX Cosmetic include:

- dry mouth
- discomfort or pain at the injection site
- tiredness
- headache
- neck pain
- eye problems: double vision, blurred vision, decreased eyesight, drooping eyelids, swelling of your eyelids, and dry eyes.
- urinary tract infection in people being treated for urinary incontinence
- painful urination in people being treated for urinary incontinence
- inability to empty your bladder on your own and are being treated for urinary incontinence. If you have difficulty fully emptying your bladder after getting **BOTOX**, you may need to use disposable self-catheters to empty your bladder up to a few times each day until your bladder is able to start emptying again.
- allergic reactions. Symptoms of an allergic reaction to **BOTOX** or **BOTOX Cosmetic** may include: itching, rash, red itchy welts, wheezing, asthma symptoms, or dizziness or feeling faint. Tell your doctor or get medical help right away if you are wheezing or have asthma symptoms, or if you become dizzy or faint.

Tell your doctor if you have any side effect that bothers you or that does not go away.

These are not all the possible side effects of **BOTOX** and **BOTOX Cosmetic**. For more information, ask your doctor or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about BOTOX and BOTOX Cosmetic:

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide.

This Medication Guide summarizes the most important information about **BOTOX** and **BOTOX Cosmetic**. If you would like more information, talk with your doctor. You can ask your doctor or pharmacist for information about **BOTOX** and **BOTOX Cosmetic** that is written for healthcare professionals.

What are the ingredients in BOTOX and BOTOX Cosmetic?

Active ingredient: botulinum toxin type A

Inactive ingredients: human albumin and sodium chloride

Manufactured by: Allergan Pharmaceuticals Ireland a subsidiary of: Allergan, Inc. 2525 Dupont Dr. Irvine, CA 92612

Allergan

This Medication Guide has been approved by the U.S. Food and Drug Administration. **Revised: 1/2016**

ATTACHMENT G

Rhode Island Department of Health
Guidance Document Regarding the Operation of Medical Spas and Intravenous (IV) Therapy Businesses

Background

The Rhode Island Department of Health (RIDOH) is charged with implementing and enforcing laws for the protection of the public's health; this expansive authority includes oversight of healthcare facilities and healthcare professionals. The statutory authority for this regulatory oversight is largely set forth in Title 5 ("Businesses and Professions") and Title 23 ("Health and Safety") of the R.I. General Laws.

In the past few years, RIDOH has seen a proliferation of two new healthcare business types – medical spas and intravenous (IV) therapy businesses.

Medical spas, sometimes referred to as medspas or medispas, offer an array of services from traditional esthetic services (e.g., hairdressing, manicures) to traditional medical procedures (e.g., Botox, fillers, laser hair removal). For the purpose of this document, the term "medical spa" means an entity that offers or performs esthetic procedures that (a) do not require sedation; and (b) are directed at improving the person's appearance; and (c) do not meaningfully promote the proper function of the body or prevent or treat illness or disease. The term also refers to an entity that offers or performs any other esthetic procedure or treatment requiring the participation of a licensed healthcare professional.

Intravenous (IV) therapy businesses provide patients with IV fluids with or without medications, vitamins, minerals and/or amino acids. Sometimes these services are offered within a medical spa, but more often are a standalone business.

The services offered in these settings are advertised as being of minimal risk and thus are treated more as spa treatments rather than medical procedures; many of which intersect the specialties of medicine, nursing, and pharmacy. This framing makes it confusing for healthcare professionals and the public to understand the responsibilities of each specialty.

Furthermore, RIDOH has discovered many of these businesses operating without proper healthcare facility licensure and/or providers performing procedures that are not within their scope of practice nor adhering to the proper standard of care. Thus, patients receiving these medical treatments in these settings are at a higher risk for complications, including inadequate results (requiring additional procedures), infections, burns, and in extreme cases, death.

Based upon the foregoing, RIDOH's Division of Healthcare Quality and Safety (DHQS) in consultation with the professional boards of licensure and discipline, issue this guidance to

provide clarity on the licensure, ownership, standard of care, and standard of practice for healthcare professionals in medical spas and intravenous (IV) therapy businesses[1].

Questions regarding this guidance should be directed to Lauren Gareau at lauren.gareau@health.ri.gov or 401-222-4525.

Medical Spa and IV Therapy Business Ownership and Licensure

As medical spas and IV therapy businesses are an agglomeration of medical disciplines, the ownership structure of these facilities varies. In some instances, a dermatologist or plastic surgeon is the owner and in others, it is an esthetician. Some are owned by unlicensed investors. Determination for licensure is complex and heavily fact-dependent and it may be best for potential owners of medical spas and IV therapy businesses to seek legal counsel.

In Rhode Island the determination for the requirement of a healthcare facility license for a medical spa or IV therapy business is based on the ownership structure, services offered, and professional licensure (if any) held by the owners of the medical spa or IV therapy business.

In the event that the owner and/or operator holds no professional license or does not qualify for an exemption via a professional service corporation, **an organized ambulatory care facility license is needed.**

Certain professional license holders (e.g., physicians, dentists, registered nurses, physician assistants) are permitted to form a professional service corporation (PSC) under R.I. Gen. Laws Chapter 7-5.1. By forming a PSC, professional license holders can be exempt from an organized ambulatory care facility license (unless providing services within a mobile unit), under R.I. Gen. Laws Chapter 23-17, if the individuals of the PSC are owning and operating the business. Individuals who form a PSC may require prior written approval of the applicable board as discussed in R.I. Gen. Laws § 7-5.1-3.

R.I. Gen. Laws § 7-5.1-3 authorizes a combination of professional licenses to form a PSC (e.g., physician and dentist). At least one individual of the PSC must be able to perform the services they are offering to qualify for the exemption from an organized ambulatory care facility license. For example, a PSC that is comprised of nurses who are offering Botox at their medical spa would not qualify for an exemption from an organized ambulatory care facility license, as nurses are not able to examine, diagnose, prescribe, or administer Botox. In this example, the group of nurses would need to include a physician, physician assistant (PA), or certified nurse practitioner (CNP) in the ownership of the PSC to be exempt from an organized ambulatory care facility license.

[1] RIDOH and the boards acknowledge and appreciate the South Carolina Department of Labor, Licensing and Regulation and the Alabama Board of Medical Examiners for addressing many of the IV therapy business issues in their well-reasoned Advisory (South Carolina, Dated August 15, 2023) and Declaratory Ruling (Alabama, dated July 21, 2022). The issues raised in both are also an accurate representation of current IV practices in Rhode Island.

In some instances, a single provider or group of providers may form a PSC to be exempt from an organized ambulatory care facility license but then hire a management company that will actively operate the business with significant influence and no active involvement of the PSC members. This "leasing" of the PSC to circumvent the need for a facility license is a misrepresentation of the purpose of the law. Such arrangements will require the management company to receive an organized ambulatory care facility license and members of the PSC who engage in such practice may have adverse action taken against their professional license.

Medical spas and IV therapy businesses who elect to use a management company remain responsible for the limited services provided by the management company.

Medical spas whose business model involves providing, arranging to provide, offers to provide or in any other way provides for the delivery of direct nursing services in the home or in a location that is not the business's brick and mortar establishment (e.g., workplace, pool side, event space), **requires a home nursing care provider (HNCP) license regardless of professional license held**. An HNCP license requires a certificate of need (CON) pursuant to R.I. Gen. Laws Chapter 23-15.

Medical spas that wish to utilize a mobile unit and perform services in a van, trailer, or other **mobile method require an organized ambulatory care facility (OACF) license.** An OACF license requires prior Initial Licensure review and recommendation by the Health Services Council pursuant to R.I. Gen. Laws §§ 23-17-14.3 and 23-17-14.4, prior to issuance of the license by the Center for Health Facilities Regulation (CHFR).

There are various ways a healthcare business, like a medical spa or IV therapy business, can be structured. RIDOH, including the professional boards, does not provide advice or guidance on such matters and individuals should seek legal counsel for those questions.

Regardless of the ownership and/or professional license of the medical spa and/or IV therapy business, neither the business nor the business owner is permitted to exercise any control over the manner in which the physician, PA, or CNP provides medical services and must not interfere in the independent exercise of the responsible practitioner's medical judgment.

Standard of Care in Medical Spas and IV Therapy Businesses

Prior to the patient receiving any service or procedure in a medical spa or IV therapy business, the patient must first be assessed by a Rhode Island licensed practitioner[2]. Only the following individuals may diagnose, treat, correct, advise, or prescribe medication (including intravenous fluids) to a person for any human disease, ailment, injury, infirmity, deformity, pain, or other medical condition:

1. A physician licensed to practice allopathic or osteopathic medicine in this state, pursuant to the provisions of R.I. Gen. Laws Chapter 5-37.

[2] For the purpose of this document, the term "practitioner" means physician, physician assistant, and/or certified nurse practitioner.

2. A licensed physician assistant who is qualified by academic and practical training to provide medical and surgical services in collaboration with physicians and pursuant to the provisions of R.I. Gen. Laws Chapter 5-54.
3. A certified nurse practitioner licensed in accordance with R.I. Gen. Laws Chapter 5-34.
    a. **Only family practice CNPs and adult gerontology CNPs are permitted to participate in medical spas and IV therapy businesses.** All other CNP foci are prohibited from participating in medical spas and IV therapy businesses as the procedures are not within their scope of practice and training.
4. A dentist licensed to practice dentistry in the state and pursuant to R.I. Gen. Laws Chapter 5-31.1.
    a. Dentistry, as defined in R.I. Gen. Laws § 5-31.1-1(6), means the evaluation diagnosis, prevention, and/or treatment (nonsurgical, surgical, or related procedures) of diseases, disorders and/or conditions of the oral cavity, cranio-maxillofacial area and/or the adjacent and associated structures and their impact on the human body.

The physician, PA, CNP, or dentist must create a comprehensive medical record that complies with the standard of care. It is critical that the practitioner obtain informed consent and document the consent in the medical record. Informed consent is an educational process involving the patient in shared decision-making during which the practitioner should be able to determine if the patient has the ability to understand relevant medical information and the implications of treatment alternatives and to make an independent, voluntary decision. The practitioner must present relative information accurately and sensitively, in keeping with the patient's preferences for receiving medical information.

In addition to informed consent, the medical record must also include:

1. Patient history;
2. Examination results;
3. Records of drugs (including intravenous fluids) prescribed, dispensed, and/or administered;
4. A diagnosis;
5. The nature and purpose of recommended interventions;
6. The burden, risks, and expected benefits of all options, including foregoing treatment; and
7. Patient's decision.

Medical records must be stored for at least seven years[3].

Some medical spas may try to circumvent the necessity of a physical assessment by a practitioner through the use of standing orders. The issuance of standing orders in this scenario, by a practitioner for a registered nurse (RN) or other provider to follow, does not satisfy the requisite provider-patient relationship. **The use of standing orders for an individualized assessment, diagnosis and treatment of patients is considered unprofessional conduct and can result in disciplinary action on one's license.**

[3] See: https://health.ri.gov/medicalrecords/

Scope of Practice and Standard of Care Requirements for IV Therapy Businesses

The services offered at an IV therapy business fall under the practice of medicine[4] and require an evaluation, diagnosis, and treatment of the patient.

As stated previously, only physicians, physician assistants, and CNPs may diagnose, treat, correct, advise, or prescribe IV medication to a person for any human disease, ailment, injury, infirmity, deformity, pain, or other condition.

It should be noted that emergency medical service practitioners (e.g., EMTS)[5], phlebotomists, licensed practical nurses, nursing assistants, medical assistants, dentists[6], podiatrists, chiropractors, veterinarians, naturopaths, and midwives are unable to provide services in these businesses as **it is outside of their scopes of practice** (i.e., diagnose, treat, prescribe, and/or administer IV fluids)**.**

In certain instances, an RN is the only licensed healthcare provider onsite at an IV therapy business. **The RN is operating outside of their scope of practice if they are diagnosing, prescribing, compounding, and/or treating the patient with IV hydration or therapy.**

While some IV therapy businesses have a physician, PA, and/or CNP owner, co-owner, investor, or associate, it may be that no practitioner evaluates the patient to make a diagnosis and prescribe a specific therapy to treat that diagnosis. Instead, the practitioner may be a "medical director," "consultant," "collaborator," "on staff," or "available" but only an RN assesses and treats the patient. This is insufficient to establish a valid practitioner-patient relationship that is required prior to the prescription and administration of drugs including IV therapies. Only licensed prescribers, namely physicians, PAs, and CNPs (only family practice CNPs or adult gerontology CNPs) can participate in an IV therapy business setting, evaluate the patient, make a diagnosis, and prescribe a treatment.

An appropriately licensed practitioner must first assess the patient (performing a history and physical exam) and document in a written medical record the assessment and plan (e.g., a diagnosis with a valid corresponding treatment regimen)[7]. Ideally, the exam is in person, as a complete medical assessment is difficult to conduct via telemedicine. For example, if a patient has signs of heart failure, listening to the heart and lungs with a stethoscope and looking for pitting edema in the lower extremities is critical, as such evidence would be a contraindication for additional fluids.

---

[4] The term "practice of medicine," as used in this document, does *not* hold the same meaning as used in R.I. Gen. Laws § 5-37-1 or the rules and regulations for *Licensure and Discipline of Physicians* (216-RICR-40-05-1).
[5] While emergency medical practitioners can administer IVs, they cannot provide IVs in an IV therapy business as emergency medical service practitioners licensure is "solely in affiliation with an ambulance service currently licensed by RIDOH unless providing care as a Good Samaritan." From the rules and regulations for *Emergency Medical Services,* 216-RICR-20-10-2.
[6] Dentists can provide IV fluids in the normal course of their dental practice. They are prohibited from providing IV fluids in IV therapy businesses.
[7] This is required regardless of whether insurance will be billed for services.

A simple questionnaire without an appropriate clinical assessment (i.e., a history and physical examination) is prohibited and may be considered professional misconduct.

The practitioner must create a comprehensive medical record that complies with the standard of care in the same manner detailed above. IV therapy businesses with a practitioner available via telemedicine must still follow the above requirements for medical records and standard of care.

It is common that when a practitioner is only available via telemedicine, the IV therapy business will utilize the NPI number of a physician, PA, or CNP to acquire necessary supplies and then use standing orders directing the administration of IVs. **The issuance of standing orders for an RN to follow does not satisfy the standard of care by a physician, PA, or CNP; and the use of standing orders for this business model is considered unprofessional conduct and may result in disciplinary action against the licensed independent practitioner.**

IV treatments need to be individualized for patients and prescribed in the same manner as an urgent care center, emergency department, or hospital.

An IV therapy business cannot remove the requirement for practitioner involvement by allowing the patient to direct their own care; and **the practitioner (or nurse) engages in unprofessional conduct by allowing the patient to select their own medications and/or IVs from a menu**.

Compounding

Generally, the operation of an IV therapy business involves walk-in patients being offered a menu of pre-selected mixtures of additives to basic IV fluids (e.g., saline). These mixtures may include amino acids, vitamins, minerals, nutrients, and some medications like famotidine, omeprazole, ibuprofen, or ondansetron. These mixtures are offered to patients, often with catchy names, for the treatment of dehydration, migraines, hangovers, nausea, athletic or postoperative recovery, appetite regulation, and/or inflammation support. In some instances, the IV therapy business may make a "custom" IV mix based on the patient's selection or examination results.

The addition of any drug(s)/medication(s), vitamin(s), mineral(s), amino acid(s,) or other substance to an IV bag is, by law, compounding. Pursuant to the rules and regulations for *Pharmacists, Pharmacies, and Manufacturers, Wholesalers, and Distributors* (216-RICR-40-15-1), compounding is defined as "[t]he act of combining two or more ingredients as a result of a practitioner's prescription or medication order occurring in the course of professional practice based upon the individual needs of a patient and a relationship between the practitioner, patient and pharmacists."

The Food and Drug Administration (FDA) defines compounding as "[t]he process of combining, mixing, or altering ingredients to create a medication tailored to the needs of an individual patient. Compounding includes the combining of two or more drugs."[8] Thus, compounding must

[8] *See*: Drug Compounding and Drug Shortages | FDA (fda.gov)

result from a valid practitioner's order in the course of professional practice and not from a patient-driven menu akin to ordering at a restaurant.

The United States Pharmacopeia (USP) is the recognized publication that contains standardized requirements for compounding, including sterile compounding found in USP <797> and has been adopted by the FDA and RIDOH as the enforceable standard. Furthermore, all compounding is also subject to the requirements outlined in the rules and regulations for *Pharmacists, Pharmacies, and Manufacturers, Wholesalers, and Distributors* (216-RICR-40-15-1).

The USP <797> applies to all persons who prepare compounded sterile preparations (CSPs) and all places where CSPs are prepared for human and animal patients. This includes, but is not limited to, pharmacists, technicians, nurses, physicians, veterinarians, dentists, naturopaths, and chiropractors in all places including, but not limited to, hospitals and other healthcare institutions, medical and surgical patient treatment sites, infusion facilities, pharmacies, and physicians' or veterinarians' practice sites.

Rhode Island law allows pharmacists to compound drugs and oversee trained personnel compounding drugs. Physicians are permitted to compound as well as delegate compounding to other healthcare professionals, provided the compounding occurs under a physician's supervision. Pursuant to the Rules and Regulations for *Licensure and Discipline of Physicians* (216-RICR-40-05-1), physicians are required to follow USP <797> and the rules and regulations for *Pharmacists, Pharmacies, and Manufacturers, Wholesalers and Distributors* (216-RICR-40-15-1) when compounding. **The regular storage, preparation, and compounding of drugs by anyone other than a licensed physician, pharmacist, or pharmacy is prohibited unless licensed by RIDOH in these professions.** IV therapy businesses that elect to compound must have a physician on-site for supervised compounding or have a licensed pharmacy on-site to prepare compounds under the supervision of a pharmacist. The physician or pharmacist supervising the compounding must be on-site; remote supervision of compounding is prohibited. An IV therapy business that does not prepare their own compounds may receive compounds from a licensed pharmacy or a federally registered outsourcing facility (i.e., 503B Outsourcing Facility).

The USP <797> "immediate use" provision governs the emergency preparation of a sterile drug product, and in certain circumstances, this provision allows for the preparation of a sterile product to be made outside of full USP compliance. In some cases, IV therapy businesses have been interpreting the concept of "immediate use" to allow the compounding of IVs to circumvent USP requirements, especially for sterility and training. The "immediate use" provision is not a workaround for the quality and safety standards that govern sterile product preparation. Walk-in or concierge IV therapy services do not fall under USP <797> "immediate use" definition.

ATTACHMENT G

Scope of Practice in Medical Spas and IV Therapy Businesses

Scope of practice for professions can be found in R.I. laws and regulations promulgated by RIDOH. With the development of new technologies and procedures, RIDOH relies heavily on the professional boards to advise on what new procedures fall within the scope of practice of each licensee.

The following chart is a visual of common procedures that are performed in medical spas and IV therapy businesses that RIDOH and the respective boards have determined are within each licensee's scope of practice, provided that such licensee has the requisite training and experience**. This list is not exhaustive and any questions about procedures not listed should be directed to the applicable board and/or to RIDOH.**

	Physician[1]	PA[1,2]	CNP[1,3]	Pharmacist	Dentist	RN	LPN	Electrologist	Esthetician	Tattoo Artist	Permanent Makeup Artist
Body Sculpting	Yes	No	No	No	No	No	No	No	No	No	No
Chemical Peels	Yes	Yes	Yes	No	No	No	No	No	Yes[7]	No	No
Cryolipolysis (Cool Sculpting)	Yes	No	No	No	No	No	No	No	No	No	No
Dermal Filler	Yes	Yes	Yes	Yes[4]	Yes	No	No	No	No	No	No
Dermaplaning	Yes	Yes	Yes	No	No	No	No	No	No	No	No
Hair Transplant	Yes	Yes	No	No	No	No	No	No	No	No	No
Inkless Stretch Mark Revision	Yes	Yes	No	No	No	No	No	No	No	Yes	Yes
Intravenous Fluids	Yes	Yes	Yes	No	No[5]	Yes[1,4]	No	No	No	No	No
Laser Hair Removal	Yes	Yes	Yes	No	No	No	No	Yes[6]	No	No	No
Laser Tattoo Removal	Yes	Yes	No	No	No	No	No	No	No	No	No
Liposuction	Yes	No	No	No	No	No	No	No	No	No	No
Microblading	Yes	Yes	No	No	No	No	No	No	No	Yes	Yes
Micro Channeling	Yes	Yes	Yes	No	No	No	No	No	No	No	No
Microneedling	Yes	Yes	No	No	No	No	No	No	No	No	No
Neuromodulators (Botox)	Yes	Yes	Yes	Yes[4]	Yes	No	No	No	No	No	No
Oxygen Therapy	Yes	Yes	Yes	No	No[5]	Yes[1,4]	Yes[1,4]	No	No	No	No
Platelet-Rich Fibrin	Yes	No	No	No	No[5]	No	No	No	No	No	No
Platelet Rich Plasma	Yes	No	No	No	No[5]	No	No	No	No	No	No
Pulsed Intense Light	Yes	Yes	No	No	No	No	No	No	No	No	No
Radio Frequency	Yes	Yes	No	No	No	No	No	No	Yes	No	No
Saline Tattoo Removal	Yes	Yes	Yes	No	No	No	No	No	No	Yes	Yes

1. Must have appropriate training in these procedures.
2. In collaboration with a physician.
3. Family practice CNPs and adult gerontology CNPs only.
4. Must have a valid prescription by a physician, PA, or CNP.
5. Dentists can provide this procedure during the course of normal dental work; however, dentists cannot perform such procedure in a medical spa and/or IV therapy businesses.
6. Must meet training requirements in accordance with R.I. Gen. Laws 5-32-21
7. The acidity of the chemical peel cannot exceed 30%.

ATTACHMENT G

Ablative lasers or ablative energy devices are intended to excise or vaporize the outer layer of skin. These procedures should only be performed by a physician or delegated to an appropriately trained PA, with training and experience in the use of these devices. Examples of ablative lasers include carbon dioxide (CO_2) lasers and erbium lasers.

Body sculpting (also known as body contouring) is the use of non-invasive means to change the shape of an area of the body. This includes the use of very cold temperatures, heat, laser, red light or radiofrequency energy to destroy fat cells. This includes the use of Zerona®, truSculpt®, CoolSculpting®, ScupltSure®, EMSCULPT neo®, Morpheus8 Body, Vanquish RF and other devices.

Chemical Peels means a procedure in which a chemical solution is applied to the skin to remove the top layers. Chemical peels are used to treat wrinkles, discolored skin, and scars. They can be done at different depths from light to deep. Deeper chemical peels offer more dramatic results but also require a longer recovery period.

Cryolipolysis, also known as "CoolSculpting®" means the use of very cold temperature to break down fat cells.

Dermal Filler means injection of synthetic substances (e.g., hyaluronic acid, calcium hydroxyapatite, polymethylmethacrylate, Poly-L-lactic acid), collagen, or fat in order to increase the amount of collagen in a body area.

Dermaplaning is a treatment in which dead skin cells and peach fuzz are scraped off with a scalpel.

Hair Transplant means the surgical technique that removes hair follicles from one part of the body, called the "doner site", to a bald or balding part of the body known as the "recipient site."

Hyaluron pens are prohibited for use. They have not been approved by the Food and Drug Administration and are not for legal sale in the United States.

Inkless stretchmark revision means a procedure that involves injecting a serum and/or vitamins into the dermis layer of the skin using a tattoo needle, causing microabrasions. It is also known as dry tattooing, medical needling, inkless needling, and MCA needling.[9] This process may also be used to improve the appearance of scars.

Intravenous Fluids means injecting liquids to a person through a vein. This includes providing stock intravenous (IV) fluids (e.g., 0.9% normal saline, lactated Ringer's solutions) with or without the addition of vitamins, minerals, amino acids, medications, etc. Intravenous fluids are, by law, drugs that must be prescribed by a licensed independent practitioner (physician, physician assistant, or CNP) for a specific patient with a specific diagnosis for which the IV fluids are indicated.

[9] A tattoo is defined as inserting a colored ink into the skin through a needle to mark or color the skin by introduction of non-toxic dyes or pigments into the skin. From the rules and regulations for *Tattoo Artists and Tattoo Parlors*, 216-RICR-40-10-16.

ATTACHMENT G

Laser Hair Removal means using a non-ablative laser to perform hair removal or reduction. It differs from electrolysis, which is the use of an electric current to destroy hair follicles.

Laser tattoo removal means a procedure that uses laser light energy to break up tattoo pigment into small particles in which the body's immune system clears over time.

Liposuction means a cosmetic surgical procedure for removing excess fat from under the skin by suction.

Microblading means a semipermanent eyebrow tattooing procedure which uses a handheld tool with tiny needles to inject pigment into the skin.

Micro Channeling means the use of ultra-fine needles to inject customized serums (often containing dermal fillers, platelet rich plasma, and/or Botox) directly into the skin.

Microneedling means the use of thin needles to make tiny holes in the top layer of skin. The damage helps stimulate the skin's healing process, so it produces more collagen and elastin (proteins that keep skin firm and smooth).

Neuromodulators (Botox) means a wrinkle-relaxing injection of botulinum toxin, commercially known as Botox Cosmetic, Dysport, Xeomin, or Jeuveau – that are used to treat wrinkles, frown lines, and crow's feet.

Non-Ablative Lasers, light treatments and energy device treatments that do not excise or vaporize the outer layer of skin, may be provided by a physician or delegated to an appropriately trained CNP or PA with training and experience in these treatments. Laser hair removal uses a non-ablative laser. An electrologist who has completed training pursuant to R.I. Gen. Laws § 5-32-21 may perform laser hair removal without physician supervision.

Oxygen Therapy means the provision of supplemental oxygen.

Platelet Rich Fibrin (PRF) means the process of harvesting one's blood and mixing it with a protein matrix called fibrin. The mixture then is turned into a gel made up of a high concentration of white blood cells, fibrin, and stem cells (growth factors) and injected into other areas of the body.

Platelet Rich Plasma (PRP) means the process of harvesting one's blood, centrifuging it to separate platelets and plasma from other blood cells and injecting the platelets and plasma back into the body.

Pulsed Intense Light means the use of light energy of multiple wavelengths to remove pigmented skin areas including age spots, facial telangiectasia (broken blood vessels), freckles, and birthmarks by focusing the energy into the dermis.

Radio Frequency means a non-surgical skin tightening procedure involving an electromagnetic device that generates heat to stimulate the production of collagen, elastin, and new skin cells.

Saline tattoo removal means injecting saline into an existing tattoo in order to dissolve the ink. This procedure may only be performed by tattoo artists and permanent makeup artists.

ATTACHMENT G

Any license type not listed above, such as nursing assistants, emergency medical service practitioners (e.g., EMTs)[10], optometrists, veterinarians, or hairdressers cannot perform any of the above medical procedures as they are not within their scopes of practice.

Persons with no professional licensing are prohibited from performing any medical procedures. **A course certificate of completion for any of the above procedures does not constitute a license**. Performing any medical procedures without a license may subject an individual to fines and/or civil or criminal penalties.

[10] While some of these procedures can be performed by emergency medical service practitioners, they cannot provide services in a medical spa setting, as emergency medical service practitioners licensure is "solely in affiliation with an ambulance service currently licensed by RIDOH unless providing care as a Good Samaritan." From the rules and regulations for *Emergency Medical Services,* 216-RICR-20-10-2.

ATTACHMENT H

ALABAMA STATE BOARD OF MEDICAL EXAMINERS
Larry D. Dixon, Executive Director

March 23, 1999

Dear :

The Alabama State Board of Medical Examiners has received and reviewed your January 14, 199, letter concerning unlicensed assistive personnel giving injections. You have asked for an Alabama State Board of Medical Examiners opinion on "physicians delegating medication administration, especially administration by injection, to unlicensed assistive personnel."

In your letter, you state that unlicensed assistive personnel in physicians' offices or clinics may be administering medications, including administering medications by injection. According to your information, the administering of medications by unlicensed personnel is occurring without the involvement of a licensed nurse. A practice consultant at the Alabama Board of Nursing has told you that the Alabama Board of Nursing has no jurisdiction over unlicensed personnel, and, therefore, could not comment on unlicensed assistive personnel giving injections when a licensed nurse is not involved. We understand that you have also requested an opinion from the Board of Nursing on the issue of whether the act of administering a mediation by injection is considered the practice of nursing and, therefore, an act which requires a license to practice as a nurse.

After reviewing applicable law, including state and Federal statutes and Alabama State Board of Medical Examiners' Rules, it is clear, concerning physicians and unlicensed personnel, that only the physician has the authority to make the decision to provide medication, by injection or otherwise, to a patient. This decision-making authority should never be delegated to unlicensed assistive personnel.

There exists no Alabama State Board of Medical Examiners' Rule which addresses the act or task of injecting patients with medication by unlicensed assistive personnel. Consequently, if unlicensed assistive personnel in a physician's office or clinic administer medication by injection to a patient pursuant to delegation by the physician and under the direct supervision of the physician, it is the Board's opinion that no violation of any Board of Medical Examiners Rule has occurred; however, the physician remains responsible for the actions of the employee.

This opinion by the Board is limited to the facts and circumstances set forth in your letter dated January 14, 1999, and is issued on reliance of the correctness of those facts.

I hope that the foregoing information has been responsive to your requests.

Sincerely,
Alabama Board of Medical Examiners

/s/ William M. Lightfoot, M. D.

William M. Lightfoot, M. D.
Chairman

WML:cjh