Complications of fillers in the lips and perioral area: Prevention, assessment, and management focusing on ultrasound guidance

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Review

Complications of fillers in the lips and perioral area: Prevention, assessment, and management focusing on ultrasound guidance

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Summary An ever-increasing interest in perioral rejuvenation with dermal fillers reflects the esthetic importance of this region. However, filler injections in the lips and perioral area have been associated with various complications. Such complications are classified according to severity (mild, moderate, severe) or by the time of onset: immediate (within 24 h after injection), early (24 h to 4 weeks post-procedure), and late or delayed (> 4 weeks after injection). While most complications are mild and manageable, vascular compromise, infections, and the development of delayed-onset nodules may significantly undermine the ultimate esthetic outcome and cause substantial morbidity. These more serious complications often require more invasive treatment modalities. This article details the prevention and management of such adverse events and discusses safe filler injection principles, including safety recommendations for the lips. Lastly, we highlight the use of ultrasound guidance in complication prevention (vascular mapping, filler identification, location, and extent), assessment (identification of intravascular embolus or external vascular compression by the filler implant), and

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management (real-time imaging of hyaluronidase or other drug injection in the affected area). Esthetic practitioners should be versed in injection anatomy, and the prevention, recognition, and management of filler complications in the perioral area.

Contents

Though minimally invasive, filler injection in the lips and the perioral area has been associated with complications, even in the hands of an experienced injector.[1–3] This article discusses the prevention, assessment, and management of filler complications in the lips and perioral region focusing on ultrasound guidance.[4,5]

Methods

We have completed a narrative review as a systematic review is not feasible due to the high heterogeneity of articles on this broad topic. We searched PubMed and Google Scholar databases from inception for complications of dermal fillers in the lips and perioral region. Complication is defined as an adverse effect that emphasizes direct causality between the filler procedure and the adverse outcome or event. Key terms in the search included “complication OR adverse event,” “safety,” “prevention,” “management OR treatment OR intervention,” “hyaluronidase,” “filler,” and “perioral OR lip.” We performed separate searches for important complications using the terms “reaction,” “granuloma,” “nodule,” “infection OR biofilm,” “vascular occlusion OR vascular compromise,” “skin necrosis,” and for filler types using the terms “hyaluronic acid,” “calcium hydroxylapatite,” “silicone,” “poly-L-lactic acid,” and “polymethylmethacrylate.” A separate search for using ultrasound (key term “ultrasound”) in filler procedures was performed. We searched the reference lists of relevant articles. We included

Table 1 Soft-tissue filler complications in the perioral area.

Immediate-/early-onset (up to 4 weeks post-procedure) events
Injection site reactions[a] (pain, erythema, edema, ecchymosis, itch)
Infection (usually staphylococcal, streptococcal, or herpetic)
Hypersensitivity reactions (usually Type I)
Non-inflammatory papule/nodule (contour irregularity)
Skin discoloration/Tyndall effect
Vascular compromise/skin necrosis
Late-onset (4 weeks to years post-procedure) events
Edema
Persistent discoloration
Hypersensitivity reaction (usually Type IV)
Infection (usually mycobacterial/biofilm-related)
Inflammatory nodule
Foreign body granuloma
Migration of filler implant

[a] Commonly occurring adverse events.

expert opinions, panel recommendations, and professional body guidance.

Classification of complications

Filler complications can be classified according to severity (mild, moderate, severe), nature (ischemic, nonischemic), or by the time of onset (immediate, early, delayed).[2] Immediate (within 24 h after injection) and early (24 h to 4 weeks after injection) complications are listed in Table 1. In a systematic review of 3965 patients treated on the lips with hyaluronic acid (HA) filler, pain, swelling, bruising, papules, redness, and itching were the main presentations.[6] Most complications were mild (71–88%). Late-onset or delayed (> 4 weeks after injection) complications (Table 1) are due to filler migration, soft-tissue edema, granulomatous inflammation, fistulae, or fibrosis.[7,8] Complications can also be classified according to their etiology/pathogenesis into bleeding-related, allergy/hypersensitivity-related, granulomatous and immune-mediated, infectious/inflammatory, vasoocclusive, and inappropriate technique-related (overcorrection, migration, and malposition). Complications associated with symptomatic aggravation include painful lip hardening, infection, nodule formation, lip function impairment affecting speech or eating, and lip hypo-/hyperesthesia.

Injection-site complications

These are primarily mild and last a few days.

Ecchymosis

Ecchymosis (bruising) is usually observed after injection of the filler material by the fanning or threading method and typically disappears within a week. It can be minimized by slow injection of the filler material and cold compresses throughout and after the procedure. When possible, anticoagulant therapy should be discontinued before the procedure. Arnika, Aloe vera, and vitamin K creams have been used to treat postoperative bruising.[2,9]

Pain and edema

The edema (swelling) may be secondary to immunoglobulin E (IgE)-mediated type I or a delayed-type IV hypersensitivity.[2] Late-onset edema, likely caused by a delayed hypersensitivity, has been reported.[10] Pain and swelling can be minimized by applying ice (cold compresses) prior to and throughout the injection using a small gauge needle or blunt cannulas and using fillers mixed with lidocaine.[11] Preprocedure medications such as bromelain and arnica may help prevent swelling.[2] Nonsteroidal anti-inflammatory drugs can help ameliorate moderate postprocedure pain and swelling. Severe swelling may require the use of a course of low-dose oral steroid. Mild erythema is commonly noted after the injection, but persistent erythema may require a short course of moderate potency topical steroid.

Skin discoloration

Several types of skin discoloration have been observed in the late period, including neovascularization, hyperpigmentation, and the Tyndall effect.[2] Neovascularization occurs because of the tissue trauma caused by the filler injection and may resolve within 3–12 months without treatment – vascular laser or intense pulsed light therapy can help in challenging cases. Hyperpigmentation is more common in skin phototypes IV to VI and is typically noted at the cutaneous lip. It may be caused by hemosiderin deposition related to tissue trauma from the injection, for example, bruising secondary to high injection speed or fanning injection, or multiple puncture injection technique. The most effective therapy for persistent hyperpigmentation is a combination of a lightening agent, such as topical hydroquinone, daily broad-spectrum sunscreen and sun protection, and chemical peel[2]; intense pulsed light and lasers have also been utilized. Pigmentary change with liquid silicone presents a therapeutic challenge.[12]

Inappropriate injection technique-related complications

Inappropriate injection technique for a specific anatomic site, for example, injecting a high filler volume or placing filler in the wrong tissue layer, can cause complications such as visible implants, palpable nodules, and overcorrection.[13,14]

Tyndall effect

When particulate HA fillers are inappropriately injected too superficially, a bluish discoloration (Tyndall effect) can result and may persist for a long time.[2] Treatment with up to

75 international units (iu) of hyaluronidase (HYAL) can be effective[15] – a smaller number (10–20 iu) is required if a small amount of HA needs to be sculpted.[11] It is advisable to follow up with the patient in 3–4 days to check whether additional HYAL should be utilized. If HYAL treatment is inadequate, a q-switched Nd:Yag laser can be used.[16] As a last resort, a thin (30-gauge) needle or #11 scalpel can be used to express the filler as long as 12 months post-injection.[15]

Nodule formation

Nodules are classified into noninflammatory, inflammatory, or infectious.[2] Early-onset nodules are generally painless and noninflammatory and result from suboptimal injection techniques such as excess filler use in an area with thin skin (e.g., the wet-dry vermillion border), superficial injection, and use of incorrect filler material for the indication–filler migration often results (Figures 1 and 2). Early-onset noninflammatory nodules can be massaged and monitored. If they do not subside within 1–2 weeks, they can be treated with needle aspiration, incision with evacuation, or HYAL injection.[9,17] Early, red, painful, nonimproving nodules usually signal a concomitant infection.[18] They should be treated promptly with oral antibiotics, and the area should not be massaged to minimize the spread of the infection.[14] Incision and drainage should be performed if the area is fluctuant, and the material expressed should be sent for culture.

Delayed-onset nodules (DONs)

DONs are usually inflammatory (i.e., immune response to filler material; Figure 3), granulomatous (on histology), or related to infection/biofilm.[19] A review identified a 0.5% incidence of DON formation with a median time of onset of 4 months and a median time to resolution of 6 weeks.[20] A skin biopsy and microbiological testing should rule out granuloma formation and infection. The management of DONs caused by HA fillers is detailed in Figure 4.

Granuloma

Granuloma (Figure 5) (incidence 0.01–1%) typically appears after a latent period, which can be several months to years post-injection.[21,22] The diagnosis should be confirmed histologically. Although the material expressed is usually culture negative, biofilm formation has been a suggested trigger.[14] Factors that increase the risk of granuloma formation include nonbiodegradable fillers, the large size of a permanent filler such as polymethylmethacrylate (PMMA), large injection volumes, and previous infection/trauma at injection sites.[23] Granulomas can be treated with HYAL dosed up to 150 iu/ml.[2] They may also respond to oral/intralesional steroids.[24] A high dose, for example, 20–40 mg/ml of intralesional triamcinolone, is required as lower doses seem to create resistance and increase the risk of recurrence.[7] The combination of intralesional triamcinolone

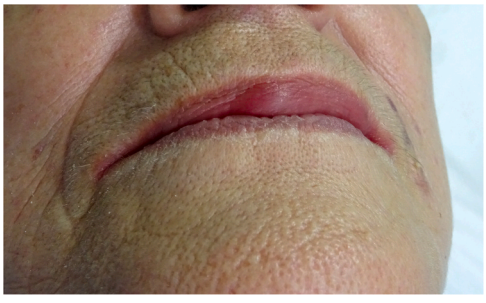

Figure 1 A nodule on the vermillion body of the upper lip is shown; it was noted as a delayed complication of liquid silicone injection to the upper lip.

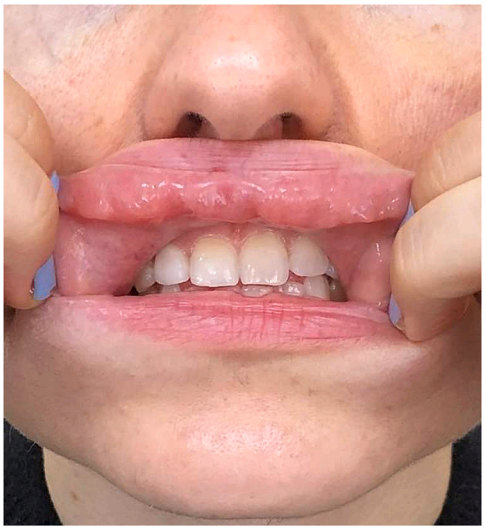

Figure 2 HA filler migration to the mucosal aspect of the upper lip. This complication was due to a combination of poor technique and overfilling.

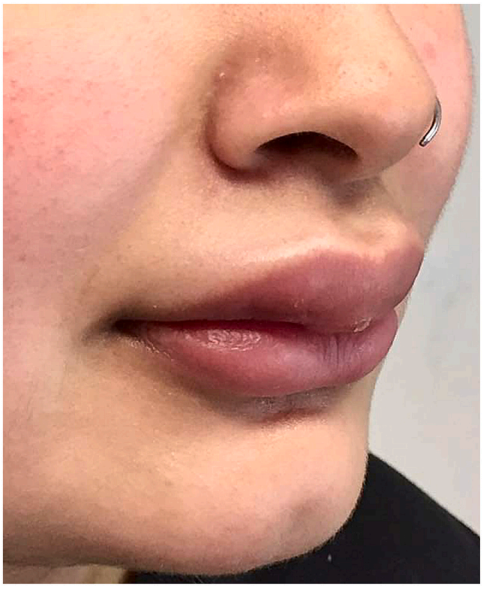

Figure 3 An Inflammatory nodule on the upper body vermillion was noted as a late complication, and it appears that it was due to an immune reaction to the HA product.

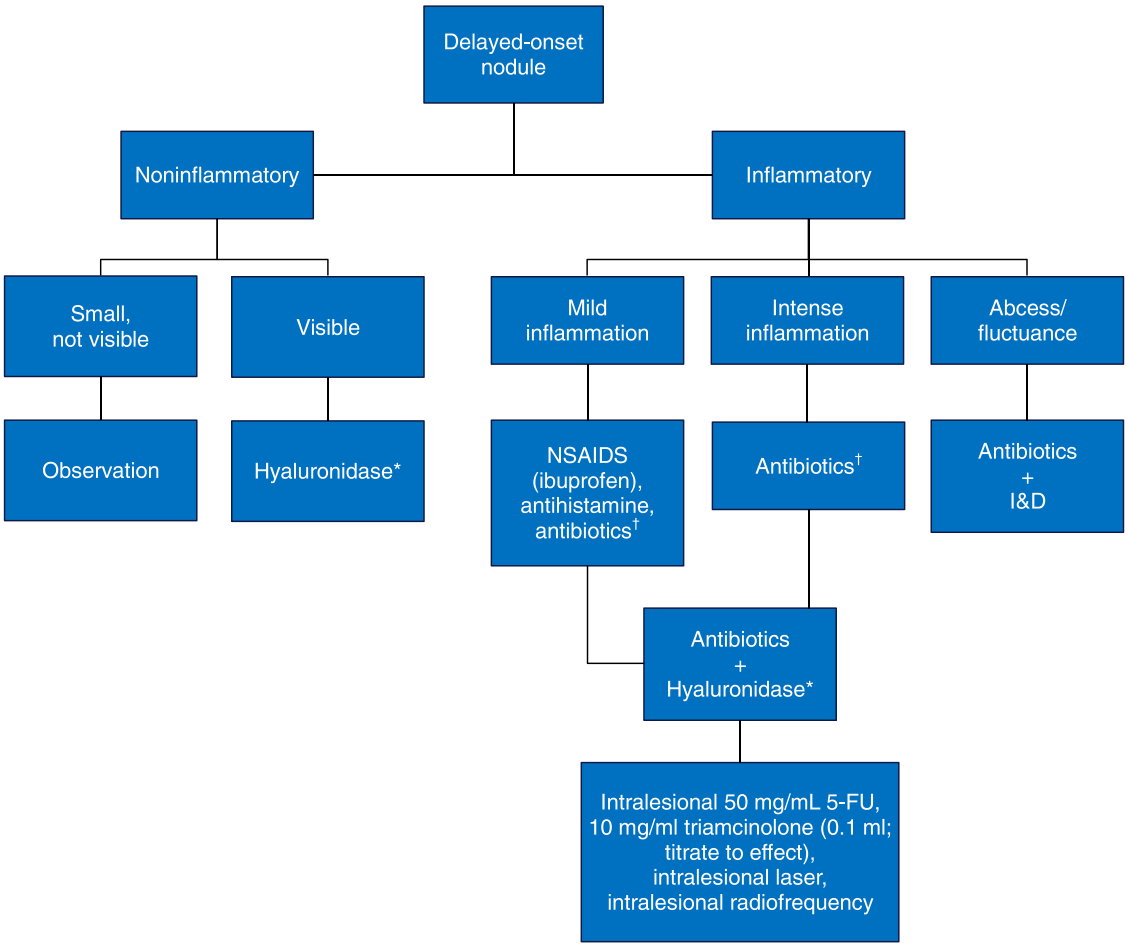

Figure 4 Summary of management strategies for delayed-onset nodules caused by HA fillers. Inflammatory nodules originate potentially from infection. *Hyaluronidase dose may vary based on the area treated. †Antibiotic therapy should be administered for 2 weeks before hyaluronidase injection. 5-FU, 5-fluorouracil; I&D, incision and drainage; NSAIDS, nonsteroidal anti-inflammatory drugs.
Figure modified from Philipp-Dormston et al. Plast Reconstr Surg Glob Open. 2020.[13]

10 mg/ml, 5-fluorouracil (5-FU) 50 mg/ml, and lidocaine appears to diminish the risk of skin atrophy associated with higher triamcinolone doses.[7] Treatment should be repeated at regular intervals until resolution. Surgical excision is the last resort.

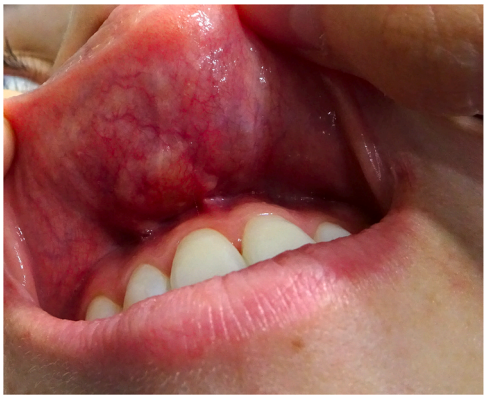

Figure 5 A nodule in the submucosa of the upper lip was noted 4 months after injecting HA in the upper lip.

Allergic and hypersensitivity reactions

Most reactions are localized.[12] The manifestations include edema, induration, and erythema at the injection site, pruritus, pain/tenderness, and eruption as early as a few days and as late as years after injection[18]; systemic manifestations are uncommon.[12] Type I hypersensitivity reactions, such as localized angioedema, are uncommon and can be treated with oral antihistamines.[25] In severe episodes or antihistamine-resistant cases, a short course of oral corticosteroid can be administered.[26] Keeping an emergency kit containing epinephrine pens, oral corticosteroids, and antihistamines in the treatment room is advisable.

Type IV (delayed) hypersensitivity reactions are noted in less than 1% of cases,[27] and can manifest with painful erythematous nodules.[18] Most authors concur that a pretreatment skin test is not essential. The pathogenesis of these reactions may be related to the presence of protein contaminants in the filler material.[26] Delayed reactions do not generally respond to antihistamines, and removal of the allergen is often the only option for resolution.[14]

COVID-19 vaccine-triggered delayed inflammatory reaction to HA filler

Such reaction presents clinically as edema with inflammatory, erythematous nodules at the site of prior HA filler injections within 10 days after mRNA COVID-19 vaccination.[28-31] Marked improvements were noted within 5 days of lisinopril 5–10 mg administration in all patients.[29,30] It has been suggested that angiotensin-converting enzyme 2 (ACE2) inhibitors, such as lisinopril, can block ACE2 receptor targeting by the SARS-CoV-2 spike protein that releases a proinflammatory T helper 1 (Th1)-mediated reaction to incipient granulomas.[29,30] A case was treated with HYAL injection.[32] The American Society for Dermatologic Surgery guidance indicates that patients with HA filler do not have any contraindication to receiving the COVID-19 vaccine, and those already vaccinated remain candidates for future receipt of HA filler.[33]

Infections/biofilms

Filler injection breaks the skin barrier, which increases the infection risk. Bacterial, mycobacterial, viral, and fungal infections have been observed post-filler injections.[18] Reactivation of herpes simplex virus infection is nearly exclusively encountered in lip augmentation—it can be prevented by delaying the procedure in patients with active infection and providing oral antiviral prophylaxis starting one day before and completing three days after filler injection.[34] Dental procedures done in the vicinity of dermal fillers may result in complications such as infections that can mimic a dental infection.[21]

Acute bacterial infections present as inflammation or abscess and are typically due to *Staphylococcus aureus* or *Streptococcus pyogenes*.[2] Delayed-onset and chronic infections may involve *Escherichia coli* and mycobacteria. It is clinically challenging to distinguish inflammation secondary to infection/biofilm from a low-grade hypersensitivity reaction such as a granuloma. In the former, antibiotic therapy that covers atypical mycobacteria should be started, whereas, in the latter, corticosteroid therapy should be considered. A bacterial culture is a helpful adjunct. Although uncommon, abscess formation may occur in the late period.[14] Treatment may be prolonged with repeated courses of antibiotics and incision and drainage (Figure 4), or removal of the filler material.

When a filler procedure punctures the skin, the biofilm (aggregate of encapsulated organisms in a polymeric matrix that adheres to the skin surface) can enter deeper structures and release bacteria to cause a local infection, a systemic infection, or a granulomatous reaction. Biofilms have been linked to the development of delayed-onset complications, including nodules, cellulitis, and abscesses that can present even years after the filler injections. Bacteria in biofilms have been detected in biopsies despite negative cultures.[2] Molecular techniques such as polymerase chain reaction and fluorescence in situ hybridization can help detect bacteria in nodules where biofilm formation is suspected.[4,14] As biofilms progress, they become more resistant to antibiotics.

Management of such complications includes a prolonged course of broad-spectrum antibiotic therapy, including doxycycline and clarithromycin. HYAL should not be used in the presence of an active infection/cellulitis because it can facilitate the spread of infection into adjacent tissues.[19] In such cases, it is recommended that oral antibiotic treatment be provided for at least one week prior to hyaluronidase injection. Additional treatments for biofilms include low-dose intralesional triamcinolone mixed with 5-FU injected at regular intervals until resolution.[34] Removal of the filler material is the last resort, but often the only cure—the biofilm and painful nodule will usually resolve afterward.[35]

Vascular compromise

Vascular occlusion (VO) associated with cosmetic injection may be due to intravascular embolism, extravascular compression, and vascular spasm.[1,36] The presentation depends on the anatomic region, the caliber of vessels affected, and zones of a prior surgery with atypical vascular patterns. It can manifest with immediate blanching, hyperemia or mottling/livedo reticularis, or a dusky appearance in the skin (Figure 6). A reperfusion reaction is bound to happen, which leads to diffuse hyperemia, exudative oozing, swelling, and pain.[1]

VO in the upper lip may be mistaken for a bruise or hematoma. The patient may present with hyperemia, exaggerated edema, pain, discoloration, and later, a vesicular eruption or weeping of the skin. Such vascular insults can occur from a lateral lip injection with a needle at the plane of *orbicularis oris* muscle. A study by Cotofana and colleagues indicated that, in the paramedian lip location, the labial arteries were submucosal in 78.1%, intramuscular in 17.5%, and subcutaneous in 2.1% of specimens.[37] However, the location of these arteries at the midline was most variable. Another study showed that the superior labial artery ran in the submucosal position in 50% of specimens and intramuscular in the remaining 50%.[38] Therefore, according to these studies, the subcutaneous position is the least likely to bear the labial arteries. The dense surrounding capillary network allows the lip to heal well in most instances of vascular compromise.[1] Ors reported 16 patients (total sample 841; lip filler in 225) who presented with VO, resulting in skin necrosis.[39] All ischemic complications were confined to the nose, nasolabial, and glabella regions – the lip was unaffected. A theoretical risk of blindness from occlusion of the central retinal artery or the ophthalmic artery should be considered secondary to anastomoses of the superior labial artery branches; however, such incidence has not been reported.

Vascular compromise can occur with filler injections deep in the superficial musculoaponeurotic system or at the muscular plane in the nasolabial fold.[40,41] Intravascular injection may cause segmental hypoperfusion in the distribution of the facial artery, including the lateral segment of the labial artery and any branches along the nasolabial fold including the inferior alar artery.[1] Filler injections in this area should be immediately intradermal when treating skin creases and immediately subdermal when treating

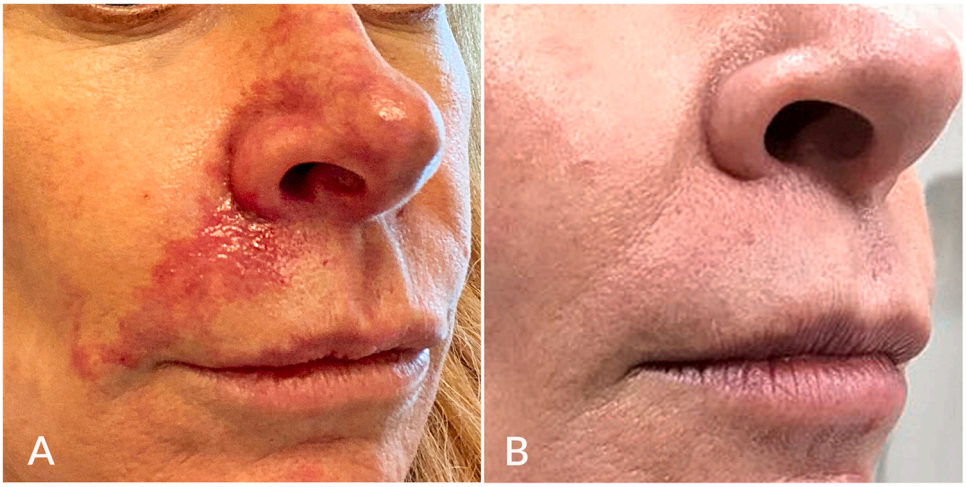

Figure 6 *A*, vascular compromise after embolization of the angular artery with HA injected in the nasolabial fold-manifested with a livedoid pattern. *B*, the complication's resolution without sequelae is shown seven days after treatment with 700 iu HYAL.

deeper folds. When injecting in the upper third of the nasolabial fold near the alar base, there is a risk of injuring and compressing the inferior alar, lateral nasal, facial, and angular arteries – injecting at the pre-periosteal level using the depot or bolus technique helps prevent such complications because the angular artery can be seen at the subdermal level in this location.[42] An alternative technique would be an intradermal injection. Using a cannula in the nasolabial fold is associated with a decreased risk of vascular complications compared to needles.

While supraperiosteal injections in the chin are considered lower risk, inadvertent injection of HA into a branch of the submental artery in the chin has been reported[43]; the deep branch passes between the muscle and bone, supplies the lip and periosteum of the mandible, and anastomoses with the inferior labial and mental arteries. Also, intravascular injection into the facial artery while injecting along the jawline in the chin area can affect vascular perfusion of the neck inferiorly and corner of the mouth superiorly. To prevent this complication, injecting the chin at the supra-periosteal plane in the region between the canines is advised.

A high-dose (450–150 iu) pulsed HYAL protocol should be adopted for vascular compromise secondary to HA filler – for example, 450 iu for an area half of the upper lip.[44] HYAL should be injected diffusely into all ischemic tissues, including the course of the vessel ("flooding the area with HYAL") and accompanied by warm compresses and vigorous massage of the areas to improve the permeability of the drug and enhance blood flow.[44,45] The injections should be repeated hourly if no clinical response is observed and signs of ischemia persist.

If CaHA filler is used, saline can be injected.[1] HYAL has been suggested as a treatment for all cases of vascular compromise, regardless of filler employed, because it can reduce edema and thus decrease vessel-occluding pressure.[46] However, in a systematic review, HYAL failed to eliminate the large area of necrosis but played a moderate role in earlier recovery in limited necrosis.[33] Other interventions include topical nitroglycerine 2% under occlusion, aspirin or low-molecular-weight heparin, sildenafil, application of medical leeches (*Hirudo medicinalis*), and hyperbaric oxygen therapy.[18,45]

Patients should be advised to return to the office immediately with any signs of vascular complication (livedoid/mottled appearance, blanching, pain) because the chances of reversing the vascular event are highest in the first 4–5 h post-procedure.

Perioral complications per filler type

HAs tend to migrate along a path of least resistance created by the needle or cannula and may cause edema as they are very hydrophilic. Injections performed from above the vermillion pointing downward to enter the vermillion have a greater tendency toward backtracking and migration. However, even small particle fillers injected below the upper lip's vermillion border can migrate superiorly onto the cutaneous lip.[1] Nodule formation can occur when an HA filler is injected near the wet-dry vermillion border or toward the wet vermillion. Repeated injections in the nasolabial folds can lead to an unnatural-looking broadening of the folds leading to a "heavier" appearance of the lower face.

Calcium hydroxylapatite (CaHa), poly-L-lactic acid (PLLA), and PMMA can cause nodules and granulomas and are not recommended for lip enhancement.[1,4] CaHA can cause edema, or asymmetries and cannot be moldered easily. Early-onset CaHA nodules may respond to sterile water injection or, in our experience, a combination of normal saline, heavy massage, and mechanical degrading with a needle or cannula. PLLA can cause granulomas and nodules, especially when injected intra- or subdermally. Early developing PLLA nodules may respond to a crack, massage, and saline injection protocol.[4] As above, late-onset CaHa, PLLA, and PMMA inflammatory nodules (granulomas) may respond to an intralesional triamcinolone/5-FU/lidocaine

combination. If no progression occurs, excision, laser, collagenase, or heat treatment may be employed.[4]

Medical-grade silicone and PMMA are reactive materials and should be avoided on the perioral areas, especially lips.[1] They tend to migrate and can become expansive and edematous after a period of senescence. Silicone injections may cause an inflammatory reaction leading to fibrosis and granuloma formation (siliconoma). HFUS is especially helpful in diagnosis as it shows a characteristic artifact, known as "snowstorm," in the subcutaneous tissue (Figure 7). Although oral/intralesional steroids, and pharmacological treatments can be tried,[47] the ultimate cure for siliconoma is usually surgical removal.[4]

Complication assessment

Imaging with high-frequency ultrasound (HFUS) is a first-line tool to identify the filler, assess its size, and exclude a soft-tissue neoplasm.[48,49] Granulomatous and fibrotic reactions can be evaluated with HFUS (Figure 8) or contrast-enhanced magnetic resonance imaging (MRI).[48] White blood cell (WBC) scintigraphy may confirm a chronic subclinical infection.[50] MRI and WBC scintigraphy can help in surgical planning. SPECT-computed tomography can identify calcifications. Infrared spectroscopy allows for definitive filler identification, but the procedure is invasive.[51,52]

An international group of physicians specializing in dermatologic ultrasound suggested a Color Doppler ultrasound for all examinations because it can differentiate between different types of lesions (solid vs. cystic; vascular vs. nonvascular).[53] The minimum frequency recommended for performing dermatological examinations is 15 MHz. The time needed for an ultrasound-guided vascular mapping varies depending on the number of skin areas examined (10–20 min on average). Patients appreciate a higher level of safety provided by the ultrasound. The cost of a portable ultrasound device is low.[54] Key points to selecting a device for dermatological ultrasound were recently reviewed.[54]

Complication prevention with ultrasound guidance

Ultrasound can help prevent complications by yielding crucial vascular mapping and identifying the filler's nature, precise location, and extent post-procedure.

Vascular mapping

Color Doppler ultrasound can support the percutaneous injection of fillers by providing information on the location of the main facial vessels; having this knowledge, the provider can inject above or below the plane of a major vessel that decreases the probability of VO.[55,56] Mapping the angular artery in the piriform region before a filler procedure in the nasolabial folds enhances safety as the artery can be superficially located. Mapping the labial arteries prior to lip injection is helpful as their location at the lip midline can be variable.[37] When injecting marionette lines, a risk of

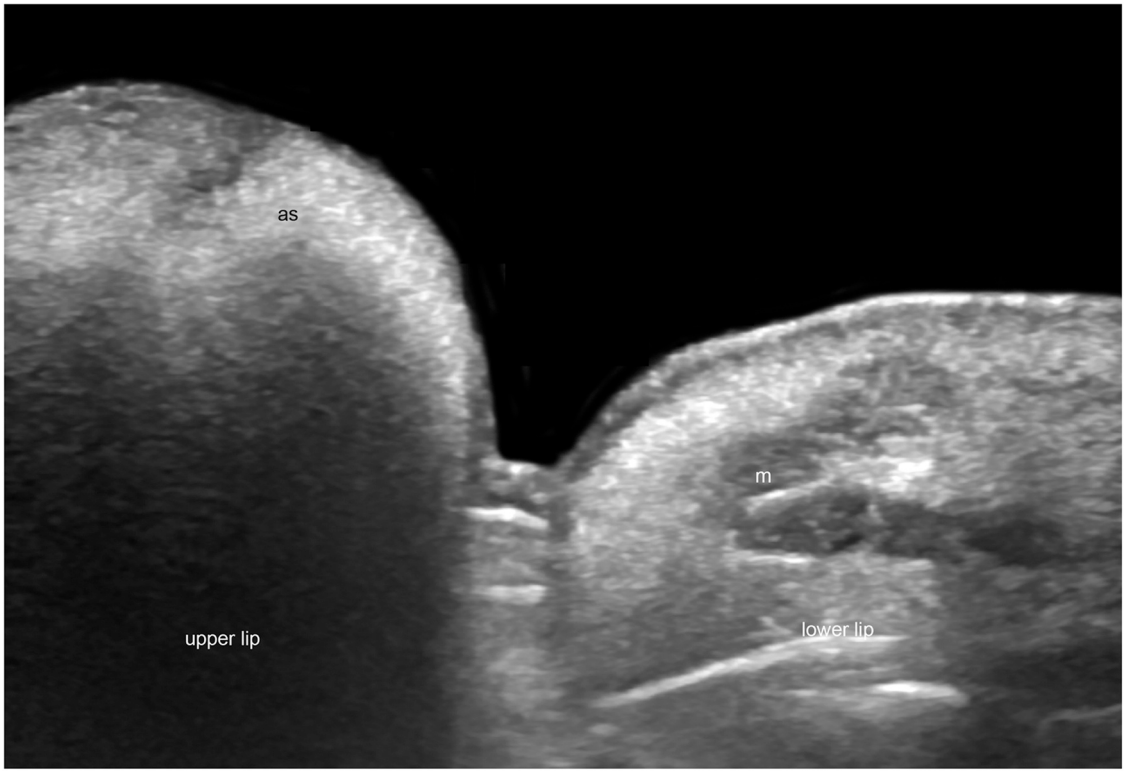

Figure 7 Ultrasound (longitudinal view; grayscale) of the lesion shown in Figure 1 demonstrates silicone oil in the dermis, subcutis, and the orbicularis muscle of the upper lip. Notice the "snowstorm" artifact generated by the silicone oil. The lower lip is unremarkable. Abbreviations: as, silicone oil; m, orbicularis oris muscle.

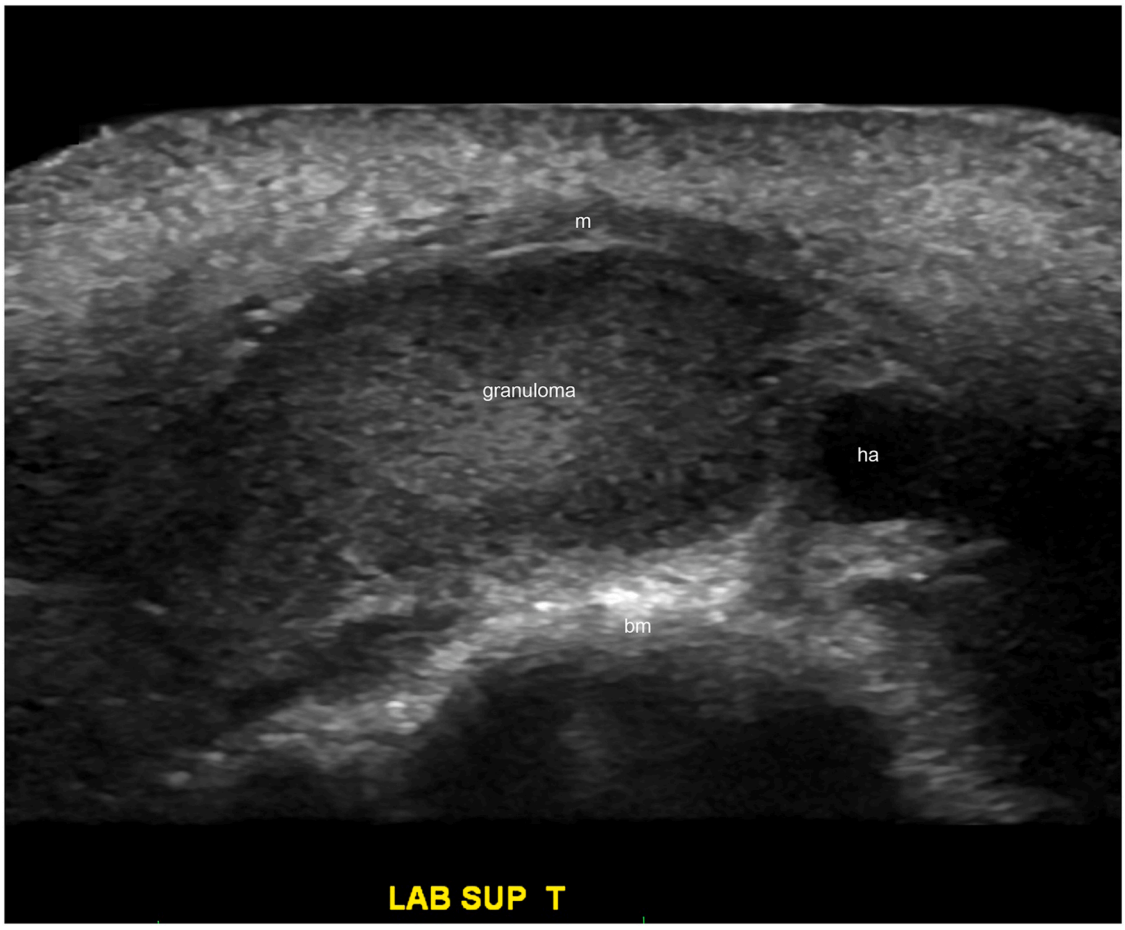

Figure 8 Ultrasound (transverse view; grayscale) of the lesion shown in Figure 5 demonstrates a submucosal and oval-shaped, hypoechoic nodule that corresponds to a granuloma and a small hyaluronic acid deposit in the periphery Abbreviations: ha, hyaluronic acid; m, orbicularis oris muscle.

injecting the filler into the facial artery exists because the vessel runs a very tortuous course as it makes its way towards the oral commissure (found 1 cm laterally to the commissure). Mapping of the chin region enhances safety because there is a risk of inadvertently injecting into the facial artery or a branch of the submental artery.[43]

Filler identification

All fillers are visible with ultrasound. Ultrasound is the first-line imaging modality for detecting cosmetic fillers.[49,55,57] Filler deposits can be identified according to their echogenicity and artifacts generated in the tissues (Table 2). Compared with MRI, ultrasound has a higher axial spatial resolution and can detect submillimeter deposits of fillers.[58] On HFUS, HA fillers appear as well-defined, regular, anechoic masses at their early stage (they do not reflect ultrasound waves because they are hydrophilic), but as they age and lose water, they become hypoechoic. The diagnosis of late complications such as chronic inflammation and granuloma can be safely made under ultrasonography, avoiding the need for biopsies and the probability of scarring, which is something valued by esthetic patients.[55,58,59]

Filler location and extent

Locating the filler and measuring its size in the tissue provides an extra layer of safety (Video 1). It is helpful to identify with ultrasound whether filler is still present in cases of persistent edema as this can improve with HYAL. Locating the filler and measuring the size of a nodule with ultrasound can help guide treatment with HYAL, especially in cases where the patient requires removal of the excess filler without losing the beneficial esthetic effect. Perez-Perez et al. showed the value of ultrasound in locating a delayed subcutaneous inflammatory reaction to HA filler of the Vycross family and performing guided management.[59]

Complication management with ultrasound guidance

The ultrasonographic evaluation can support the management of complications. Ultrasound-guided injection can increase the likelihood of response of a nodule or granuloma to HYAL or steroid ensures the treatment will be efficacious (Video 2).[60] This is particularly important when the inflamed

Table 2 Sonographic characteristics of common cosmetic fillers.

Filler	Type	Echogenicity	Duration	Comments
Pure HA	Degradable	Anechoic	3-6 mo	Decrease in size over time
HA with lidocaine	Degradable	Anechoic with prominent echoes	3-6 mo	Decrease in size over time
High-density HA	Semidegradable	Anechoic with some echoes	> 2 y	Commonly located in the deep SQ tissue of the cheeks and hands
PAAG	Semidegradable	Anechoic	Up to 18 mo	Increased echogenicity of the surrounding SQ tissue
Pure silicone	Nondegradable	Anechoic	No change over time	Similar echogenicity to silicone implants; taller than wide
Silicone oil	Nondegradable	Hyperechoic	No change over time	'Snowstorm pattern'
PMMA	Nondegradable	Hyperechoic	No change over time	Mini-comet tail posterior artifact
CaHA	Nondegradable	Hyperechoic	No change over time	Posterior acoustic shadowing artifact
PLLA*	Degradable	Diffuse hyperechogenicity of the subcutis	≥ 2 y	Anechoic deposits at the time of injection that turn to diffuse hyperechoic within days

CaHA, calcium hydroxylapatite; HA, hyaluronic acid; PAAG, polyacrylamide gel; mo, months; PLLA, poly-L-lactic acid; PMMA, polymethylmethacrylate; SQ, subcutaneous; y, Years
*PLLA is a biostimulant agent that enhances volume.
Table modified from Wortsman X. J Ultrasound Med. 2015.[55]

nodule/granuloma has a "capsule" (i.e., prominent chronic inflammatory and/or granulomatous reaction at the periphery); in such case, ultrasound can show real time that the needle or cannula injecting the medication has penetrated the "capsule" before HYAL is injected. External vascular compression has been documented with HFUS.[61] Ultrasound can help identify and effectively dissolve an intravascular embolus. When treating a vascular occlusion with HYAL, lower dosages (35–50 iu) than those employed in current protocols (≥500 iu) are necessary when Doppler ultrasound guidance is used (Figure 9).[56] Also, a single HYAL injection under HFSU guidance may support a full resolution of the vascular complication compared to hourly injections over several hours in the current, high-dose protocol.

Proactive prevention recommendations

These are summarized in Table 3.[13,19,36,62]

Recommendations for the lip region

Lip augmentation with fillers requires a meticulous injection technique and in-depth knowledge of lip anatomy including embryology (Figure 10). The filler choice should be based on proper knowledge of the properties and unique rheological characteristics of the various filler products.[63] A filler with an intermediate or low G′ prime and moderate cohesivity is best suited for injection to the lips. Small-particle HA gel is suited for lip and perioral rhytid correction as it has low density and viscosity that allow for a controlled flow, is well-moldable, and integrates smoothly with the lip tissues.[64] As HA fillers are very hydrophilic, one should avoid overcorrection.[65] If overcorrection occurs, massaging the area can help modify the outcome.[64] Mapping the crucial vessels, that is, facial, superior, and inferior labial arteries, with ultrasound, increases safety. If nerve blocks are performed, the provider should ensure that the injections do not distort the contour of the lips.

Various injection techniques have been described for the specific anatomic features of the lip, that is, vermillion border, vermillion body, philtral columns, oral commissures, and perioral rhytids.[64,65] These features should be injected appropriately to create harmony and balance with the face as a whole.[66] In males, lips tend to be flatter, wider, and more rectangular with a less pronounced Cupid's bow than in females; the gender-specific features should be maintained unless otherwise specified by the patient. Because of cutaneous aging and thinning out of all the layers, the once prominent tubercles and cupid's bow become blunted.[67] Therefore, the eversion of the upper lip and enhancement of the cupid's bow and tubercles contribute to a more efficient lip reshaping.

Breaching the vermillion border and the wet-dry border can result in cutaneous and mucosal migration, respectively; this may be a result of directly penetrating and compromising these anatomic borders or overfilling. Therefore, direct injections into the vermillion border should be performed with caution while direct injections of the wet-dry border should be avoided altogether. Still, some practitioners inject in the deeper wet mucosa in patients

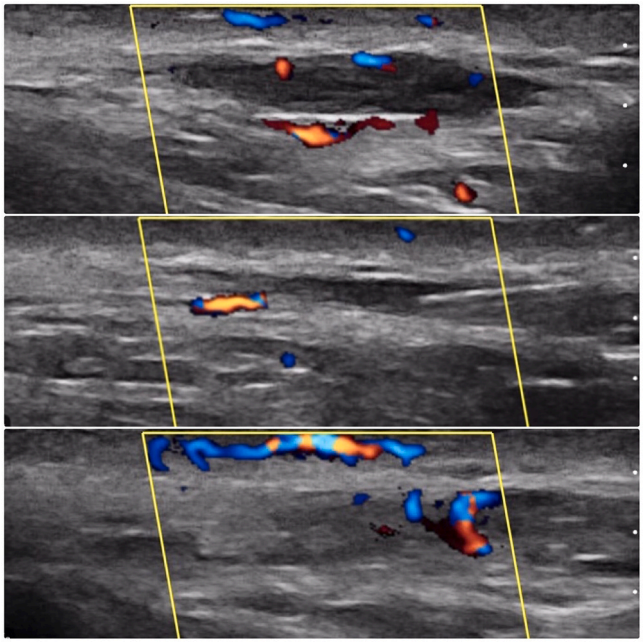

Figure 9 An example of color Doppler ultrasound use in a vascular occlusion caused by HA filler. Top: full occlusion and dilation of the vessel; middle: partial occlusion and recovery of the thickness of the vessel; bottom; full recovery of the flow and thickness of the vessel.

with very thin lips and barely visible vermillion to evert the lip (vermillion show). The risk here is compromising the labial arteries; therefore, such injection would most safely be done using ultrasound and a cannula. The safest area for injection is the dry vermillion that can hold no more than 0.3-0.5 ml of an HA filler.[64] It is recommended not to inject more than 1 ml HA into both lips (total) in a given treatment session and wait at least two weeks for further touchup treatments.

Using a cannula helps to reduce the number of needle pricks, decreasing the edema and bruising.[68,69] Most importantly, it decreases the risk of vascular complications as cannulas are less likely than needles to inject into vessels. Also, cannulas have a greater reach from a single-entry point than needles. A caveat is that the ability to fine-tune the lip shape and define the vermillion border and commissures is more limited with a cannula than a sharp needle.

The lip should be injected subcutaneously on the keratinized ("dry" side) to prevent compromising the labial arteries (Figure 10, Video 3). A linear threading technique is appropriate.[42] Lee et al. reported that the mean depth of the superior labial artery at the vermillion border ranged from 3.3 to 3.9 mm[70]; therefore, pursuing a superficial injection (i.e., < 3 mm deep) in the vermillion border helps avoid vasculature. In this context, using a short, 4-mm needle can enhance safety.[71] As the artery runs along the Cupid's bow, it can be only 1-4 mm below the vermillion border; therefore, it is important to inject very superficially in this area.[42] The entry point of the cannula should be within 1 cm medially to the commissure to minimize

Table 3 Proactive prevention recommendations.[13,19,36,62]

Patient-related factors	• Patient selection is paramount
	• Set expectations and counsel patient about potential adverse effects
	• Provide posttreatment education
Aseptic/clean procedure	• Follow sterility protocol
	• Use the smallest gauge needle possible
	• Reduce the number of piercings
	• Avoid injecting into infected/inflamed skin and through previously injected filler material
Injection technique	• Use reversible fillers (i.e., HA fillers)
	• Use thin needles (i.e., 27 G or thinner)
	• Use small syringes (0.5-1 ml) and inject small bolus (i.e., < 0.2 ml in any one region)
	• Use blunt-ended cannulas when appropriate-25 G or larger bore diameter decreases risk of intravascular injection
	• Use an anterograde/retrograde injection technique
	• Keep the needle in constant motion
	• Avoid transmucosal injections
	• Employ a slow injection technique under low pressure-injections requiring high pressure signify danger or wrong location
	• Avoid using epinephrine or products containing epinephrine as this can mask the blanching produced by an occlusion
	• Exercise caution when injecting in areas of previous trauma/scar/previous implant or avoid altogether
	• Be familiar with the pertinent three-dimensional anatomy outlined in the danger zones
Other safety tools	• Have a filler rescue kit available*

HA, hyaluronic acid; G, gauge.
*Contains epinephrine pen, oral steroid, antihistamines.

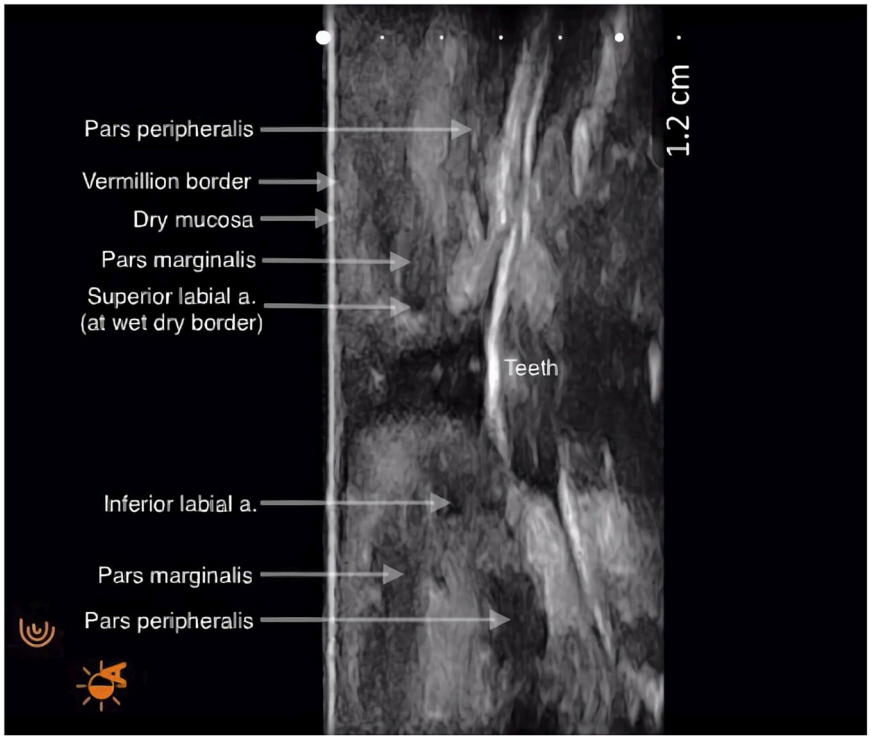

Figure 10 Ultrasonography cross-section image of the lips showing the anatomic landmarks.

the risk of compromising the facial artery. A crosshatch technique while occluding the origin of the superior labial artery by placing a thumb beside the corner of the mouth and applying lateral traction for injection helps decrease vascular risks associated with injections in the commissure.[42] Vigilance should be exercised during the injection process for local or distal blanching and sudden onset of symptoms such as severe pain or visual disturbance. If vascular compromise is suspected, the appropriate protocol should be immediately followed.[62]

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CRediT authorship contribution statement

George Kroumpouzos: Conceptualization, Data curation, Formal analysis, Writing – original draft, Writing – review & editing. **Steven Harris**: Data curation, Writing – review & editing. **Shashank Bhargava:** Formal analysis, Writing – original draft, Writing – review & editing. **Ximena Wortsman:** Data curation, Formal analysis, Writing – original draft, Writing – review & editing.

Declaration of Competing Interest

The authors declare no conflicts of interest in the materials or subject matter dealt with in the manuscript.

Appendix A. Supplementary material

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.bjps.2023.01.048.

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