An Overview of Vascular Adverse Events Associated With Facial Soft Tissue Fillers: Recognition, Prevention, and Treatment

Elie M. Ferneini, DMD, MD, MHS, MBA,* and Antoine M. Ferneini, MD

Minimally invasive facial cosmetic surgery procedures have seen an exponential increase in numbers over the past decade. The most commonly performed procedures are neuromodulator and soft tissue filler procedures. Although soft tissue fillers have a high safety and predictability profile, these procedures recently have been associated with serious and dire adverse events. This article will discuss some of the vascular complications associated with facial soft tissue fillers. Management and prevention of these adverse events also will be discussed.

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Minimally invasive facial cosmetic surgery procedures have seen an increase in numbers over the past 10 years.1 The American Society of Plastic Surgeons reported that the number of minimally invasive procedures increased 4% from 2013 to 2014.2 In fact, in 2014, the total expenditures on these procedures were almost $13 billion. The number of soft tissue procedures grew 253% from 2000. Moreover, the number of minimally invasive cosmetic surgery procedures in 2014 was 13.9 million, of which 2.3 million were soft tissue filler procedures.2 This number is expected to continue to grow. This growth has grown the interest of many oral and maxillofacial surgeons in providing facial soft tissue augmentation to their cosmetic patients.

Many of the facial fillers used today have a great safety profile with minimal adverse events.1,3,4 However, with increased clinical applications of these fillers and the increased number of procedures performed, the number of severe and detrimental adverse events is on the rise.1 This article will discuss the vascular complications, which are primarily vascular compromise and tissue necrosis.

Review of Literature

Vascular compromise after soft tissue augmentation with facial fillers is a major concern in our maxillofacial cosmetic surgical patients. This is usually related to either an intravascular injection or arterial compression that prevents blood flow through small arteries supplying the overlying skin or even the eye. In fact, certain regions of the face, such as the glabella, are at a higher risk of developing compromised blood flow and necrosis given their vascular anatomy. However, although there have been reported cases of tissue necrosis at the nasal ala, lip, and nasolabial fold areas after treatment with a hyaluronic acid (HA) or calcium hydroxyapatite,5,9 impending necrosis has been reported in cases involving all types of facial fillers with incidences estimated at 0.001% of total procedures performed. Tracy et al10 reported an
uncommon case of nasal alar and facial necrosis after calcium hydroxyapatite filler injection. Severe full-thickness necrosis of the cheek and nasal alar skin developed 24 hours after the patient underwent injection into the nasolabial folds. Ozturk et al11 performed a literature search to identify the facial sites most susceptible to severe complications. They actually found 41 articles, representing 61 patients with severe complications. Data collected from these case reports included the filler type, injection site, complication site, symptom interval, symptom of complication, time to therapy, modality of treatment, and outcome. The most common injection site for necrosis was the nose (35.3%), followed by the nasolabial fold (31.2%). Blindness was most often associated with injection of the glabella (50%). An estimated incidence of 0.0001% for the development of a severe complication was calculated. Kassir et al12 discussed a case report with extensive necrosis after injection of an HA filler. They concluded that early recognition of vascular necrosis and compromise is ideal to manage this complication. In addition, surgeons should have specific protocols for treatment after injection necrosis to improve the outcome of wound healing. Alam and Dover13 performed a Medline-based review on the management of complications and sequelae associated with injectable facial fillers. They found that injectable nonpermanent facial fillers are extremely safe. Attention to injection technique further minimizes the low risk of adverse events, which are usually minor, spontaneously resolving, and easily treated.

Glaich et al14 discussed injection necrosis of the glabella. They concluded that injection necrosis in the glabellar region may be prevented by knowledge of the local anatomy and an understanding of its pathophysiology. In addition, this complication can be treated by a post-injection protocol.

Blindness is a dire adverse event of soft tissue fillers. Beleznyay et al15 performed a literature review that identified all the cases of vision changes from facial fillers in the world literature. They reported 98 cases of vision changes from fillers. The sites that were at high risk of 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 HA fillers (23.5%). The most common symptoms were immediate vision loss and pain. Most cases of vision loss did not recover. No treatments were found to be consistently successful in treating blindness. Beleznyay et al concluded that although the risk of blindness from fillers is rare, it is critical for injecting surgeons to have a firm knowledge of the vascular anatomy and to understand key prevention and management strategies. Li et al16 investigated the possible route by which the injected filler droplets reach the ophthalmic artery. They performed a search of cases that involved visual loss due to a cosmetic facial filler injection. They found that when injecting the glabellar or forehead region, a retrograde injection into the supraorbital artery or supratrochlear artery may cause occlusion of the ophthalmic artery. While surgeons are injecting the nasolabial fold and nasol dorsal regions, any injections into the anastomosis of the dorsal nasal artery, angular artery, and lateral nasal artery can lead to a retrograde embolism. Similarly, in the temporal region, an anastomosis between the frontal branch of the superficial temporal artery from the external carotid artery and the supraorbital artery from the ophthalmic artery can lead to blindness. This can explain the accompanying brain infarction seen in patients after iatrogenic visual loss. If the injecting pressure is forceful enough, it may push the embolic materials into the middle cerebral artery. Li et al concluded that although iatrogenic ophthalmic artery occlusion is a rare complication after facial filler injections, it is devastating. They recommended that both the patient and the surgeon should be aware of the risk of irreversible blindness. Kim et al17 reported the case of a 23-year-old man with cerebral infarction and permanent visual loss after injection of an HA filler for augmentation rhinoplasty. The patient was actually admitted to the hospital with complaints of blindness in the right eye, right facial paralysis, and paralysis of the left limbs with severe pain during injection of the soft tissue filler. Brain magnetic resonance imaging (MRI) and computed tomography showed ophthalmic artery obstruction and right middle cerebral artery infarction. Acute thrombolysis was performed to treat the infarction; however, the patient’s condition did not improve. A repeat brain computed tomography scan 24 hours after thrombolysis showed intracerebral hemorrhage in the right temporal, frontal, occipital, and parietal lobe; a subarachnoid hemorrhage; and a midline shift. The patient underwent an emergency decompressive craniectomy. After the operation, the patient continued to have drowsiness, with no improvement in visual loss and motor weakness. The authors concluded that surgeons who administer facial filler injections should be familiar with the possibility of accidental intravascular injection and should explain the adverse effects of fillers to their patients.

**Discussion**

Vascular compromise after a soft tissue filler injection is a major complication that is almost always the result of an intravascular injection into an artery. This causes an embolism that impedes blood flow. All maxillofacial surgeons should have a thorough knowledge and understanding of facial anatomy. Recognition of a vascular event and aggressive
treatment are necessary to avoid potentially irreversible complications.\textsuperscript{14,16,18,19} Injection of a filler into an artery can cause necrosis of tissues in both an anterograde and retrograde fashion. Over the past 10 years, there have been a few reports of acute vision loss and hemiplegia after autologous facial fat injection as a result of ocular and cerebral embolism, respectively.\textsuperscript{20,21} An acute fatal stroke also has been reported after autologous fat injection into the glabellar area.\textsuperscript{22} In all these cases, it is thought that fragments of the fatty tissue reached the ocular and cerebral arteries via reverse flow immediately after the injection and resulted in an embolism. In addition, there are several case reports that have shown that injections at the dorsum of the nose and glabella are associated with embolization, leading to vision loss.\textsuperscript{6,19,23,24} This is primarily because of the filler microspheres traveling in a retrograde manner through the supratrochlear or dorsal nasal artery to the ophthalmic artery and then to the central retinal artery via the anterior and posterior long ciliary arteries.\textsuperscript{25}

Signs and symptoms of an arterial occlusion usually develop immediately to within hours after injection. These include immediate or early blanching, as well as severe pain. A retinal embolus is a dire complication and can present with severe pain, headache, acute vision loss, ptosis, and ophthalmoplegia. Some reports have indicated an erythematous and violet reticular discoloration at the injection site before pain, visual changes, and headache. Management of this adverse event should include emergent transfer of the patient to a hospital setting. The patient should undergo a formal ophthalmologic examination, imaging (MRI), and further workup. An MRI scan allows localization of the obstruction or embolus. A funduscopic examination may show a pale optic disc with a cherry-red spot consistent with a central retinal artery occlusion. Treatment for these patients should be aimed at lowering intraocular pressure and vasodilation (Table 1).\textsuperscript{6,19,25} In fact, decreasing intraocular pressure increases retinal perfusion in an attempt to propagate the embolus distally and minimize the amount of visual loss. Immediate lowering of intraocular pressure includes acetazolamide, 500 mg intravenously or orally. Hyperbaric oxygen treatment may be beneficial if begun within 2 to 12 hours of symptom onset. In general, the management of an arterial occlusion should be aimed at breaking the focal obstruction and improving the blood supply (Table 2).\textsuperscript{26}

Injection-induced necrosis is a rare but dreaded complication associated with the use of soft tissue fillers.\textsuperscript{1,14} Necrosis can occur from interruption of the vascular supply to the area, potentially by compression or injury. It usually results from obstruction of the affected vessel or vessels through injection directly into an artery, causing an embolism that impedes blood supply.\textsuperscript{8,14} Areas most vulnerable are those in which blood supply depends on a single arterial branch, such as the glabellar and nasolabial folds. To avoid this serious and potentially irreversible complication, oral and maxillofacial surgeons should have a heightened awareness of the possibility of vascular compromise when using fillers. Surgeons should look at and document areas of skin breakdown and have an established management protocol.\textsuperscript{3,4,25,27} Some of the signs and symptoms of tissue necrosis can vary from an early acute pain to a delayed dull pain.

Management of a tissue necrosis should begin by early recognition of this adverse event. Signs of early compromise include regional blanching of the skin in the distribution of the underlying vasculature. Necrosis can potentially affect any area of the face. Once it is recognized, the surgeon must apply warm compresses and massage the area. Warm compresses should be applied for 5 to 10 minutes every 30 minutes. This leads to improved vascular dilation and increased blood supply to the injured area.\textsuperscript{28}

### Table 1. TREATMENT OF RETINAL EMBOLUS

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<td>Lower intraocular pressure</td>
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<td>- Digital ocular massage</td>
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<td>- Topical glaucoma medications (β-blocker: timolol maleate; lopidine 0.5% ophthalmic solution [Alcon Laboratories, Inc., Fort Worth, TX])</td>
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<td>- Diuretic: acetazolamide (Diamox, 500 mg orally or intravenously [Teva Pharmaceuticals, North Wales, PA])</td>
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<td>- Induce vasodilation</td>
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<td>- Have patient breathe in a paper bag</td>
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<td>- Aspirin regimen: aspirin, 325 every day or twice a day</td>
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<td>- Emergency ophthalmology consultation or evaluation</td>
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### Table 2. MANAGEMENT OF ARTERIAL OCCLUSION

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<td>- Stop injection immediately.</td>
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<td>- Attempt aspiration of filler if possible.</td>
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<td>- Massage the area.</td>
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<td>- Apply warm compresses.</td>
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<td>- Apply 2% nitroglycerin paste.</td>
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<tr>
<td>- If the filler is an HA, inject hyaluronidase.</td>
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<tr>
<td>- If areas of skin breakdown develop, start administration of antibiotics.</td>
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<td>- Perform frequent follow-up: general supportive care and monitoring for secondary infection.</td>
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Massaging allows breaking the focal obstruction. If the filler is an HA, hyaluronidase should be used to reverse and dissolve the HA. This is a soluble enzyme that degrades HA and is a key advantage that HA fillers have over the other types of facial fillers. Hyaluronidase (eg, Vitrase [Bausch & Lomb, Rochester, MN]) should be used as early as possible, and its administration can be repeated every 60 minutes if no improvement is observed (Fig 1). Topical nitroglycerin paste (2%) should be used in the affected area. Nitroglycerin leads to vasodilation. This ultimately leads to improved blood supply and can limit the area of tissue necrosis. Aspirin also is recommended to improve blood supply to the compromised area as well as to prevent further clot formation due to vascular compromise. This regimen should be continued until clinical improvement and resolution of the area of necrosis occur. Maxillofacial surgeons should treat tissue necrosis in a timely manner (Table 3). Surgeons should have a crash cart easily accessible to manage these adverse events in an appropriate and timely way (Table 4). With increased adverse events, prevention of these complications can be accomplished. Table 5 reviews some recommendations for safe injection. In-depth knowledge of facial anatomy is a key factor for preventing complications. Marking the patient’s face before injection is a critical step in avoiding adverse events. For

**Table 3. MANAGEMENT OF IMPENDING TISSUE NECROSIS**

- Massage the area.
- Apply warm compresses.
- Apply 2% nitroglycerin.
- If the filler is an HA, inject hyaluronidase.
- If areas of skin breakdown develop, start administration of antibiotics.
- Perform conservative debridement of necrotic tissue.
- Perform incision and drainage if no improvement occurs or abscess develops.
- Start administration of aspirin, 325 mg every day.
- If there is a massive area of necrosis, consider hyperbaric oxygen treatment.

example, drawing a vertical line from the medial canthus to the oral commissure when performing nasolabial fold augmentation allows the surgeon to avoid injection into the angular artery. All injections should remain lateral to this line (Fig 2). In addition, extreme caution should be used when injecting areas of large vessels, including the following (Fig 3)12:

- Angular artery
- Supratrochlear artery
- Supraorbital notch and foramen
- Infraorbital foramen

Other techniques to avoid vascular injections include the following1,4,14,33-35:

- The viscosity of the soft tissue fillers can be reduced by premixing the material with lidocaine. However, most of the available fillers are already premixed with lidocaine.
- A less viscous facial filler can be used, if possible.
- Epinephrine should be avoided because it can result in early blanching, which can be confused with a vascular occlusion or compromise.

Aspiration before injection should always be performed. This will prevent a vascular injection.
- Injections should be performed serially and superficially, especially in the nasolabial folds and glabellar areas. This will avoid inadvertent injection into the angular and supratrochlear arteries.
- The number of injection sites should be minimized. This ultimately leads to less risk of vascular injury.
- If the surgeon is concerned about a vascular injection, pressure can be applied to occlude the proximal vessels to the injection site.

Demand for soft tissue facial fillers will continue to increase. Although these procedures are safe, potentially debilitating long-term vascular injuries can occur. Early recognition, timely management, and close follow-up are essential in treating these dire

Table 4. CRASH CART CONTENTS

- Warm compresses
- 2% nitroglycerin paste
- Aspirin, 325 mg
- Hyaluronidase
- Diamox, 500 mg
- Iopidine 0.5% ophthalmic solution
- Medrol dose pack or dexamethasone (or both) (Pfizer, Inc., New York, NY)

Table 5. RECOMMENDATIONS FOR AVOIDING ADVERSE EVENTS

- Have knowledge of facial anatomy.
- Use appropriate injection techniques.
- Use the smallest needle that still allows for accurate injection.
- Avoid rapid injection, rapid flow rates, and high volumes.
- Minimize the number of injection sites.
- Make sure patients understand follow-up instructions.
- If possible, limit use of anticoagulants and antiplatelets (consider discontinuing anticoagulants and antiplatelets if using high volumes of fillers).
- Select an appropriate filler for the treated area (depending on the type, size, and depth of defect).
- Do not overfill or overtreat.
complications. To decrease these adverse events, oral and maxillofacial surgeons should have an in-depth understanding of facial anatomy, proper patient selection, proper filler selection for the deficient area, and predictable injection techniques. Finally, improving the safety of these procedures allows for decreased adverse events and improved patient satisfaction.

References

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