

Hyaluronidase in Aesthetic Plastic Surgery: Clinical Uses, Safety, Ultrasound Guidance, And Current Controversies

Marisela Silva García*¹, Cristian Sandoval Cervantes¹

¹General Surgery, Universidad Nacional Autónoma de México.

ABSTRACT

ABSTRACT: Hyaluronic acid fillers are widely used in aesthetic medicine because of their favorable safety profile, versatility, and relative reversibility. Hyaluronidase has therefore become an essential rescue agent for the management of hyaluronic acid filler-related complications, ranging from elective correction of overfilling, nodules, migration, persistent edema, and Tyndall effect to urgent treatment of vascular compromise. Despite its widespread use, important controversies remain regarding optimal dosing, timing, injection technique, ultrasound guidance, allergy testing, filler-specific responsiveness, and the management of vision-threatening complications. This narrative review summarizes the current evidence on hyaluronidase in aesthetic practice, with emphasis on mechanism of action, available formulations, clinical indications, dosing strategies, ultrasound-guided treatment, safety considerations, medicolegal implications, and unresolved controversies. Available evidence supports early and decisive hyaluronidase administration for suspected vascular occlusion caused by hyaluronic acid fillers, whereas elective indications require a more conservative and individualized approach. Ultrasound-guided hyaluronidase is emerging as a valuable tool for precise diagnosis and targeted treatment, particularly in complex or vascular cases. However, the lack of universally accepted protocols highlights the need for standardized training, prospective studies, and practical algorithms tailored to aesthetic clinicians and injectors.

KEYWORDS: Hyaluronidase; Hyaluronic Acid Fillers; Dermal Filler Complications; Vascular Occlusion; Ultrasound-Guided Injection.

ARTICLE DETAILS

Published On:
03 July 2026

Available on:
<https://ijmscrs.com>

INTRODUCTION

The use of hyaluronic acid fillers has increased substantially in aesthetic plastic surgery because these products provide immediate volume restoration, facial contouring, and soft-tissue rejuvenation with relatively low procedural morbidity. Their popularity is also related to the perception that hyaluronic acid fillers are reversible through enzymatic degradation with hyaluronidase. However, this reversibility should not be interpreted as absolute protection against complications, particularly when vascular compromise, delayed recognition, or vision-threatening events occur [1,2]. Hyaluronidase has become a key therapeutic agent in aesthetic practice for both elective and emergency indications. Elective use includes the correction of overfilling, asymmetry, superficial product placement, Tyndall effect, persistent edema, filler migration, and selected nodular reactions. Emergency use is primarily directed

toward suspected vascular occlusion, where delayed treatment may lead to tissue ischemia, skin necrosis, scarring, or permanent functional and aesthetic sequelae [1,3-5].

Despite its clinical importance, hyaluronidase use remains highly variable. Differences exist in the selected dose, dilution, timing, injection plane, need for repeat administration, preference for blind versus ultrasound-guided technique, and approach to allergy testing. Aesthetic practitioners also differ in their use of hyaluronidase in elective versus emergency scenarios, reflecting the lack of universally accepted protocols [6]. In addition, commercially available hyaluronic acid fillers differ in their concentration, cross-linking technology, cohesivity, and resistance to enzymatic degradation, which may influence the amount and frequency of hyaluronidase required [7-9].

For plastic surgeons, hyaluronidase should be understood not only as a corrective agent but also as an essential component

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of complication preparedness. Proper use requires knowledge of facial vascular anatomy, recognition of early ischemic signs, familiarity with filler behavior, availability of emergency protocols, and careful documentation. This review aims to summarize the current evidence regarding hyaluronidase use in plastic surgery, focusing on its clinical applications, dosing strategies, injection techniques, ultrasound guidance, safety profile, medicolegal relevance, and ongoing controversies.

METHODS

A narrative review of the literature was performed using PubMed as the primary database. The search was conducted up to May 2026 and focused on articles published between 2020 and 2026 addressing hyaluronidase use in aesthetic medicine, plastic surgery, hyaluronic acid filler complications, vascular occlusion, ultrasound-guided hyaluronidase, filler degradation, dosing strategies, and safety considerations. Search terms included “hyaluronidase,” “hyaluronic acid fillers,” “dermal filler complications,” “vascular occlusion,” “aesthetic medicine,” “plastic surgery,” “ultrasound-guided hyaluronidase,” “filler-induced ischemia,” and “hyaluronidase dosing.”

Included articles consisted of narrative reviews, scoping reviews, systematic reviews, meta-analyses, experimental studies, clinical studies, case series, preliminary reports, and clinical guidance articles relevant to aesthetic plastic surgery

and filler-related complications. Articles not directly related to hyaluronidase use in aesthetic practice, duplicate publications, and papers without accessible bibliographic information were excluded. Because this was a narrative review, no formal meta-analysis or risk-of-bias assessment was performed.

Mechanism of Action and Formulations

Hyaluronidase is an enzyme that degrades hyaluronic acid by cleaving glycosidic bonds within the polysaccharide structure, thereby reducing viscosity and increasing tissue permeability. In aesthetic practice, this enzymatic activity is used to dissolve exogenous hyaluronic acid filler deposits and to facilitate the resolution of filler-related complications [3]. Its therapeutic effect depends not only on the amount of enzyme administered but also on the biochemical characteristics of the filler, including concentration, degree of cross-linking, particle structure, cohesivity, and tissue integration [7-10].

The basic mechanism of hyaluronidase-mediated filler degradation is illustrated in Figure 1 [11]. After injection, hyaluronidase diffuses through the surrounding tissue and comes into contact with the hyaluronic acid filler. The enzyme then progressively disrupts the filler matrix, breaking it down into smaller fragments that can disperse within the tissue and subsequently undergo physiological clearance.

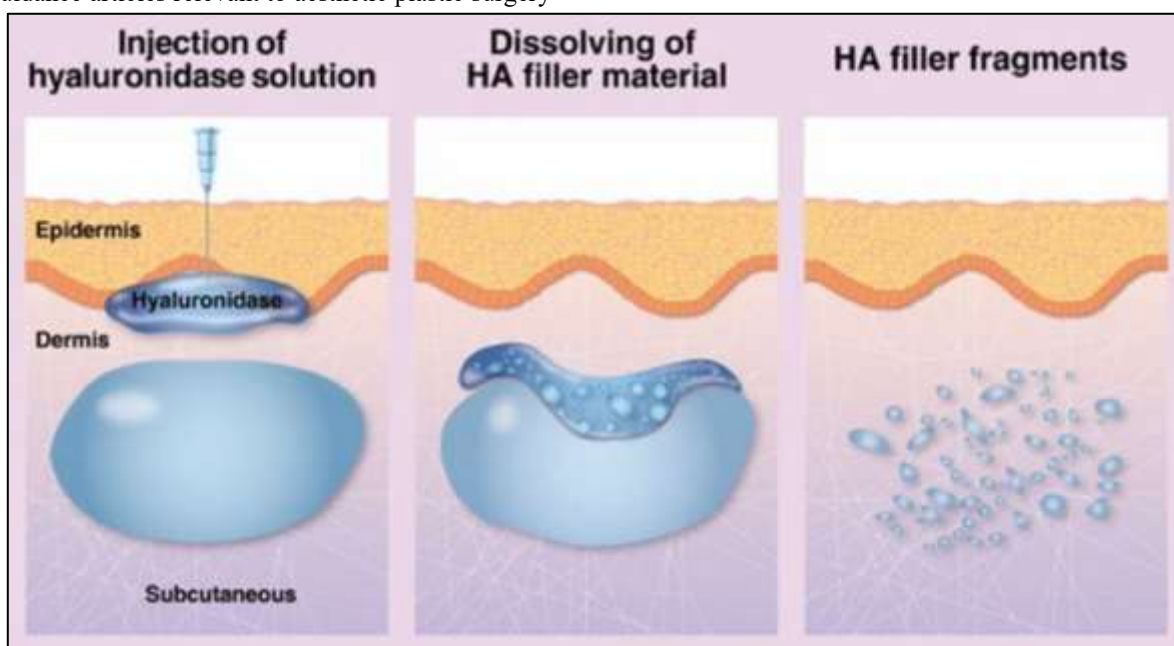


Figure 1. Mechanism of hyaluronidase-mediated degradation of hyaluronic acid filler.

Schematic illustration of hyaluronidase-mediated degradation of hyaluronic acid filler. After injection into the tissue, hyaluronidase comes into direct contact with the filler material and progressively breaks it down into smaller fragments, facilitating dispersion and tissue clearance. Reproduced from Hong and Yi [11] under the Creative Commons Attribution 4.0 International License.

Several hyaluronidase formulations have been described, including animal-derived preparations and recombinant human hyaluronidase, although availability varies by country and clinical setting. The distinction between animal-derived and recombinant preparations is clinically relevant because differences in enzymatic activity, diffusion, immunogenicity, and degradation efficiency may influence treatment response [8,12]. In vitro comparisons have demonstrated that ovine and

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recombinant human hyaluronidase may differ in their ability to degrade specific hyaluronic acid fillers, supporting the concept that hyaluronidase response is not uniform across products or formulations [8,12].

The resistance of fillers to enzymatic degradation is another important consideration. Studies evaluating commercially available fillers have shown time- and dose-dependent degradation patterns, with some fillers requiring higher doses or repeated exposure to achieve meaningful dissolution [7-10]. This variability is highly relevant in clinical practice, where an inadequate dose may fail to restore perfusion in vascular occlusion, while excessive dosing in elective correction may result in overcorrection, contour irregularity, or patient dissatisfaction.

Clinical Applications in Plastic Surgery

The clinical applications of hyaluronidase in plastic surgery can be divided into elective and emergency indications. Elective indications include overcorrection, asymmetry, superficial placement of filler, Tyndall effect, persistent edema, filler migration, and selected nodular reactions related to hyaluronic acid products [1-3]. In these settings, hyaluronidase is usually administered in a controlled manner, with conservative dosing and reassessment after treatment to avoid excessive dissolution.

Overcorrection and aesthetic dissatisfaction represent common elective scenarios. Patients may present with excessive volume, contour irregularity, unnatural projection, or asymmetry after hyaluronic acid filler injection. In these cases, hyaluronidase can be used to partially or completely reduce the undesired filler effect. However, treatment should be individualized because complete dissolution is not always necessary and may produce secondary volume loss or dissatisfaction [1-3,6].

The Tyndall effect occurs when hyaluronic acid filler is placed too superficially, producing a bluish or grayish discoloration of the skin. Hyaluronidase may be effective in dissolving superficial filler deposits and improving discoloration. Similarly, persistent edema, particularly in the periorbital and midface regions, may be related to lymphatic compromise, hydrophilic properties of the filler, or product migration; in selected cases, hyaluronidase can improve swelling and restore contour [1,3,11].

Nodules and delayed inflammatory reactions require more cautious evaluation. Not all nodules after filler injection are caused solely by accumulated hyaluronic acid. Differential diagnoses include infection, biofilm-related inflammation, granulomatous reaction, immune-mediated delayed inflammatory response, or injection of a non-hyaluronic acid material. In such cases, hyaluronidase may be useful when hyaluronic acid filler is confirmed or strongly suspected, but it should not replace appropriate evaluation for infection or other inflammatory etiologies [2,3].

The most important emergency indication for hyaluronidase is suspected vascular occlusion. Clinical findings may include immediate or delayed pain, blanching, livedo reticularis, delayed capillary refill, dusky discoloration, mottling, and progressive ischemic changes. In this setting, early recognition and immediate treatment are critical to prevent tissue necrosis and permanent scarring [4,5].

Dosing Strategies

Dosing remains one of the most debated aspects of hyaluronidase use in aesthetic plastic surgery. Current evidence suggests that the required dose varies according to the indication, severity of complication, filler type, amount of filler injected, anatomical region, time since injection, and whether the treatment is elective or emergent [1,7,12-15].

For elective correction, such as overfilling, asymmetry, Tyndall effect, superficial deposits, or mild persistent edema, conservative dosing is generally preferred. The objective is controlled correction rather than complete dissolution. In these cases, gradual treatment with reassessment is important because overcorrection may create contour deformities, volume deficiency, or patient dissatisfaction [1,3,6].

Before selecting a hyaluronidase dose, clinicians should recognize that treatment response is influenced by both product-related and patient-related variables. The amount of enzyme required may vary according to the physicochemical properties of the filler, the anatomical site, the clinical indication, the severity of vascular compromise, and whether ultrasound guidance is available. Therefore, dosing should be individualized rather than based on a single universal protocol (Table 1) [1,3,5,7].

Table 1. Factors influencing hyaluronidase dose response.

Factor	Clinical relevance
Filler concentration	Higher HA concentration may require greater enzymatic exposure.
Cross-linking degree	More highly cross-linked fillers may be more resistant to degradation.
Cohesivity and rheology	More cohesive products may dissolve more slowly or incompletely.
Time since injection	Older filler deposits may be more integrated into tissues.
Amount of filler injected	Larger volumes may require repeated treatment.

Anatomical region	Periorbital, nasal, and midface regions require particular caution.
Indication	Elective correction generally requires lower doses than vascular compromise.
Severity of ischemia	More severe vascular compromise may require urgent and repeated dosing.
Hyaluronidase formulation	Ovine and recombinant human products may differ in degradation behavior.
Ultrasound guidance	May allow more precise delivery and potentially reduce unnecessary dosing.

This table summarizes the main variables that may influence hyaluronidase dose response in aesthetic filler complications. Product-related factors include filler concentration, cross-linking, cohesivity, and rheologic behavior, whereas clinical factors include time since injection, anatomical location, severity of ischemia, hyaluronidase formulation, and availability of ultrasound guidance [1,3-5,7]. HA: hyaluronic acid.

In contrast, suspected vascular occlusion requires urgent and more aggressive treatment. The goal is not aesthetic refinement but restoration of tissue perfusion. Therefore, repeated dosing may be required until clinical improvement is observed. Systematic reviews and management protocols emphasize that treatment should not be delayed while waiting for confirmatory imaging when clinical suspicion is high [4,5]. In these scenarios, underdosing may be more dangerous than overtreatment because persistent vascular compromise can progress to necrosis.

Experimental and clinical studies have demonstrated that hyaluronic acid fillers show variable responses to hyaluronidase. Some products degrade rapidly, whereas others require higher doses, longer exposure, or multidose administration [7-10]. Studies evaluating multiple hyaluronic acid gels have further confirmed that filler composition and rheologic characteristics influence enzymatic degradation [12-15]. These findings support a clinically important principle: hyaluronidase dosing should not be considered universal across all fillers.

A practical approach is to distinguish between low-risk elective correction and high-risk ischemic complications. Elective cases may be treated with small, targeted doses and scheduled reassessment, whereas vascular compromise

requires immediate treatment, repeat administration, and escalation according to clinical response. The absence of standardized dosing protocols remains a major limitation in current practice and highlights the need for prospective studies comparing dose, dilution, timing, and clinical outcomes [1,5,6].

Injection Techniques

Several injection techniques have been described for hyaluronidase administration, including direct injection into palpable or visible filler deposits, regional infiltration, the flooding technique, and ultrasound-guided injection. The choice of technique depends on the indication, severity, anatomical location, availability of imaging, and experience of the injector [1,3,6,16].

Direct injection is commonly used for elective correction of localized filler deposits, contour irregularities, nodules, or Tyndall effect. This approach is most appropriate when the filler is superficial, palpable, or clearly localized. It allows conservative dosing and targeted correction, but it may be less effective when filler is diffuse, migrated, deeply located, or poorly defined clinically [1,3].

The effectiveness of hyaluronidase depends on adequate contact between the enzyme and the hyaluronic acid filler. Therefore, the injection plane and distribution pattern are important technical considerations. As illustrated in Figure 2 [11], hyaluronidase may be injected along the outer surface of a filler deposit or directly into the filler mass. Intralesional injection may improve enzymatic contact in well-defined filler collections, whereas broader or peripheral infiltration may be useful when the filler is more diffuse or irregularly distributed.

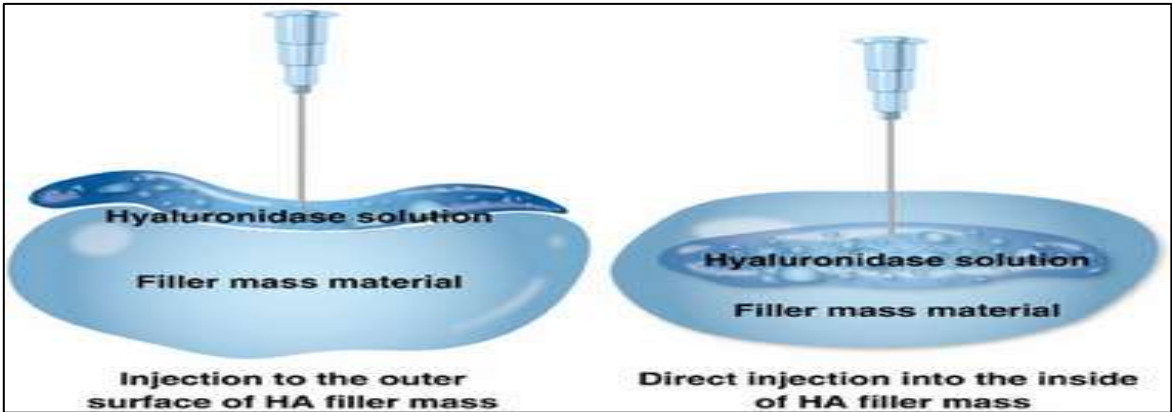


Figure 2. Injection techniques for hyaluronidase administration into hyaluronic acid filler deposits.

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Schematic representation of two approaches for hyaluronidase administration into hyaluronic acid filler deposits. Peripheral injection along the outer surface of the filler mass may allow gradual diffusion of the enzyme into the deposit, whereas direct intralesional injection delivers hyaluronidase into the filler material itself, potentially increasing enzyme–filler contact. The technique should be selected according to filler localization, depth, distribution, clinical indication, and injector experience. Adapted from Hong and Yi [11] under the Creative Commons Attribution 4.0 International License.

The flooding technique is frequently used in suspected vascular occlusion when immediate treatment is required and ultrasound is not available. This technique involves infiltrating hyaluronidase broadly throughout the affected ischemic area and along the presumed vascular territory. Its advantage is speed and practicality in urgent scenarios. However, it is less precise, may require larger doses, and can increase the likelihood of unnecessary dissolution of surrounding filler or endogenous hyaluronic acid [1,4,5].

Ultrasound-guided injection allows visualization of filler deposits, vascular structures, and, in some cases, vascular flow before and after treatment. This technique can improve diagnostic accuracy and help direct hyaluronidase to the

precise location of filler accumulation or vascular compromise [16-18]. However, it requires appropriate equipment, training, and availability. Importantly, ultrasound should not delay treatment when vascular occlusion is clinically evident and imaging is not immediately accessible [4,5].

Ultrasound-Guided Hyaluronidase

Ultrasound-guided hyaluronidase represents an important recent developments in the management of hyaluronic acid filler complications. High-frequency ultrasound can help identify filler deposits, determine their depth and anatomical relationship to vessels, differentiate hyaluronic acid from other materials, and guide precise injection of hyaluronidase [16-18].

In suspected vascular compromise, ultrasound guidance may be particularly helpful because it allows real-time visualization of the filler deposit, adjacent vessels, and Doppler flow before and after hyaluronidase injection [16]. As shown in Figure 3, targeted ultrasound-guided administration can be used to deliver hyaluronidase directly to the area of filler-related arterial flow impairment, with immediate Doppler confirmation of flow restoration after treatment.

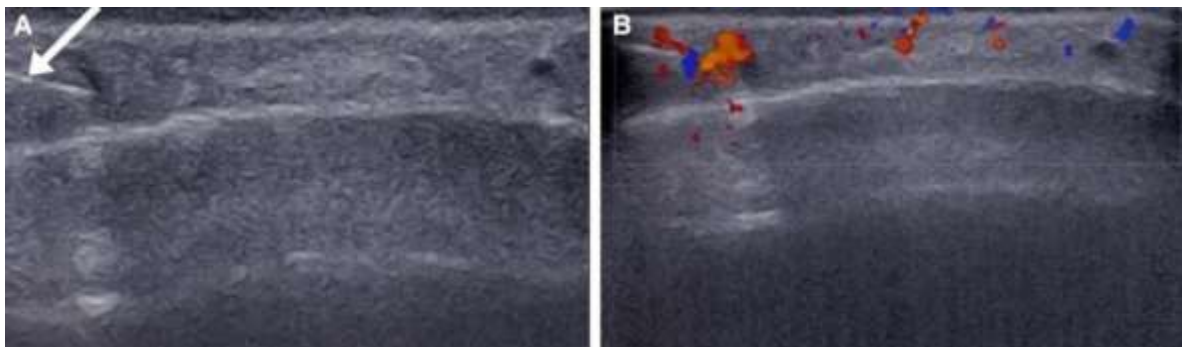


Figure 3. Ultrasound-guided hyaluronidase injection for filler-induced vascular occlusion.

(A) Ultrasound-guided injection of hyaluronidase into a hyaluronic acid filler deposit associated with arterial flow impairment. The needle is advanced under real-time ultrasound visualization to target the filler deposit adjacent to the affected vessel. (B) Immediate restoration of arterial flow demonstrated by color Doppler ultrasound after targeted hyaluronidase administration. Reproduced from Ugo et al. [16] under the Creative Commons Attribution 4.0 International License.

In elective scenarios, ultrasound may be particularly useful for patients with prior filler treatments, unclear product location, deep filler deposits, persistent edema, migration, or nodules. By improving localization, ultrasound-guided treatment may reduce unnecessary enzyme exposure and allow more conservative correction. This is especially relevant in anatomically delicate regions such as the periorbital area, nasolabial fold, lips, and midface [16,17].

In vascular compromise, ultrasound may help identify filler-related arterial obstruction and guide targeted administration of hyaluronidase. Preliminary reports and systematic reviews suggest that ultrasound-guided hyaluronidase may be associated with favorable outcomes in filler-induced ischemia and impending skin necrosis [16-18]. The potential advantages include confirmation of diagnosis, precise delivery, lower required doses in selected cases, and objective reassessment of vascular flow after treatment.

Nevertheless, the role of ultrasound as a universal standard remains controversial. Its benefits depend on operator expertise, equipment availability, and the ability to perform imaging without delaying urgent treatment. In suspected vascular occlusion, treatment should be initiated immediately when ultrasound is not readily available. Therefore, ultrasound-guided hyaluronidase should be viewed as an emerging and highly valuable tool, but not as a reason to postpone emergency management [4,5,17,18].

Ocular Complications and Vision Loss

Vision-threatening complications after hyaluronic acid filler injection are rare but devastating events in aesthetic practice. Visual loss may occur after inadvertent intra-arterial injection, followed by retrograde embolization and subsequent obstruction of the ophthalmic or retinal arterial circulation. High-risk anatomical regions include the nose, forehead, glabella, temple, nasolabial fold, and upper midface, reflecting their vascular connections with the ophthalmic arterial system [1-3,19].

A recent report by the American Academy of Ophthalmology reviewed ocular complications associated with injectable soft tissue fillers and identified hyaluronic acid as the most frequently implicated material in reported cases of filler-associated vision loss. The same report found that the nose, forehead, glabella, temple, and upper midface were among the most commonly involved injection sites, supporting the concept that central and upper facial regions represent higher-risk anatomical zones [19].

The role of hyaluronidase in ocular complications remains highly controversial. In contrast to cutaneous vascular occlusion, where early hyaluronidase administration is widely accepted as a key intervention, its ability to reverse established filler-induced visual loss remains uncertain. Reported interventions for ocular vascular occlusion have included local, orbital, retrobulbar, and intra-arterial hyaluronidase, as well as thrombolysis, anterior chamber paracentesis, corticosteroids, mannitol, and hyperbaric oxygen; however, available evidence suggests that these treatments are usually ineffective in restoring vision once retinal ischemia has occurred [19]. Therefore, hyaluronidase should not create a false sense of security when injecting high-risk facial areas.

Because randomized controlled trials are not ethically or practically feasible in this setting, current recommendations rely mainly on case reports, small case series, expert opinion, and algorithm-based approaches. Snozzi et al. proposed an evidence-informed algorithm for the management of central retinal artery occlusion following hyaluronic acid filler injection, organized into outpatient and in-hospital management steps [20]. This approach emphasizes early recognition, rapid escalation of care, urgent ophthalmologic referral, and coordinated multidisciplinary management rather than reliance on a single rescue intervention.

For aesthetic clinicians, prevention remains the most important strategy. Safe injection principles include detailed knowledge of facial vascular anatomy, use of small aliquots, low injection pressure, avoidance of large boluses in high-risk areas, continuous awareness of tissue blanching or pain, and immediate cessation of injection if visual or neurologic symptoms occur. Sudden visual disturbance, ocular pain, ophthalmoplegia, ptosis, pupillary abnormalities, headache, nausea, or neurologic deficits after filler injection should be treated as an emergency requiring immediate ophthalmologic and, when appropriate, neurologic evaluation [19,20].

Overall, ocular complications highlight the limits of hyaluronidase as a rescue agent. While hyaluronidase is essential in the management of cutaneous vascular compromise caused by hyaluronic acid fillers, its efficacy in established filler-induced blindness remains unproven. Consequently, the safest approach is prevention, early recognition, immediate referral, and structured emergency management [19,20].

Safety, Allergy, and Skin Testing

Hyaluronidase is generally considered safe when used appropriately, but adverse reactions can occur. Common local effects include erythema, edema, tenderness, bruising, pruritus, and transient discomfort at the injection site. These effects are usually mild and self-limited. More serious hypersensitivity reactions are uncommon but clinically important, particularly in patients with prior exposure to hyaluronidase or potential sensitivity to animal-derived formulations [1-4,11].

Allergy testing remains controversial. In elective cases, particularly when large doses are anticipated or when the patient has a history suggestive of hypersensitivity, skin testing may be considered. However, the predictive value of skin testing is not absolute, and a negative test does not fully exclude the possibility of hypersensitivity. In emergency vascular occlusion, treatment should generally not be delayed for skin testing because the risk of irreversible tissue necrosis may outweigh the potential risk of allergic reaction [1,3,6].

The formulation used may also influence immunologic considerations. Recombinant human hyaluronidase may have theoretical advantages over animal-derived formulations, although availability varies by country and clinical setting. Comparative studies between ovine and recombinant hyaluronidase suggest that formulation differences may influence degradation behavior and should be considered when interpreting dose-response expectations [8,12].

Plastic surgeons should maintain preparedness for allergic reactions when administering hyaluronidase, especially in emergency settings where higher or repeated doses may be needed. This includes documenting allergy history, monitoring the patient after administration, and having emergency medications and resuscitation protocols available.

Current Controversies

Several unresolved controversies continue to influence the clinical use of hyaluronidase in aesthetic plastic surgery. Although hyaluronidase is widely accepted as an essential agent for the management of hyaluronic acid filler-related complications, there is still no universal consensus regarding optimal dose, dilution, timing, injection technique, need for skin testing, formulation selection, or management of vision-threatening events. These uncertainties are particularly relevant because hyaluronidase is used in two very different clinical contexts: controlled elective correction and urgent treatment of vascular compromise [1,3,5,6].

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Because the therapeutic goal differs substantially between elective filler correction and emergency reversal of vascular compromise, current recommendations should be interpreted according to the clinical scenario rather than as a single standardized protocol. In elective cases, treatment is usually guided by the size, depth, and palpability of the filler deposit,

whereas suspected ischemic complications require immediate intervention, close reassessment, and repeated treatment when perfusion does not improve. The principal areas of controversy and their current practical interpretation are summarized in Table 2 [1,3,5-7,13-18].

Table 2. Current controversies in hyaluronidase use for hyaluronic acid filler complications.

Controversy	Current interpretation
Optimal dose	No universal dose exists; dosing depends on indication, filler type, severity, and clinical response.
Low-dose vs high-dose strategy	Low doses may be appropriate for elective correction; higher or repeated doses are favored in vascular compromise.
Blind injection vs ultrasound guidance	Blind or flooding techniques are practical in emergencies; ultrasound improves precision when immediately available.
Need for skin testing	May be considered in elective cases, but should not delay treatment of vascular occlusion.
Formulation differences	Ovine and recombinant human hyaluronidase may differ in degradation behavior and immunogenicity.
Filler-specific resistance	Different hyaluronic acid fillers respond differently depending on cross-linking, cohesivity, and concentration.
Effect on native hyaluronic acid	Temporary degradation of endogenous hyaluronic acid is possible, but its clinical significance remains debated.
Use in nodules	Useful when nodules are hyaluronic acid-related; inappropriate if infection, biofilm, or non-hyaluronic acid material is present.
Role in vision loss	Efficacy in established filler-induced blindness remains unproven.
Medicolegal access	Any clinician injecting hyaluronic acid fillers should have immediate access to hyaluronidase and an emergency protocol.

Dosing remains the most persistent controversy. Although conservative dosing is generally appropriate for elective correction of overfilling, asymmetry, Tyndall effect, or localized filler deposits, suspected vascular occlusion requires a more urgent and aggressive approach. In ischemic complications, repeated administration may be necessary until there is objective clinical improvement in pain, skin color, capillary refill, and tissue perfusion. However, there is no universally accepted protocol defining the optimal amount, dilution, frequency, or endpoint of treatment [1,5-7,13-15].

Another major controversy is whether all hyaluronic acid fillers respond similarly to hyaluronidase. Available evidence indicates that fillers do not degrade uniformly. Fillers differ in concentration, cross-linking technology, cohesivity, rheologic behavior, and resistance to enzymatic degradation. These differences challenge the concept of a single standardized dose and support an individualized approach based on filler characteristics, anatomical location, and severity of the complication [7-15].

The choice of injection technique is also debated. The flooding technique remains practical and rapid in suspected vascular occlusion, especially when ultrasound is

unavailable. However, ultrasound-guided hyaluronidase offers greater precision by allowing visualization of filler deposits, vascular structures, and, in selected cases, restoration of flow after treatment. Its limitations include the need for equipment, operator training, and immediate availability. Therefore, ultrasound guidance should be considered a valuable adjunct but should not delay treatment in clinically obvious vascular compromise [4,5,16,17].

Allergy testing represents another unresolved issue. Skin testing may be reasonable in selected elective cases, particularly when there is a history suggestive of hypersensitivity or when large doses are anticipated. However, in suspected vascular occlusion, delaying hyaluronidase administration for allergy testing may be harmful. In this setting, the potential benefit of immediate treatment generally outweighs the theoretical risk of hypersensitivity, provided that appropriate monitoring and emergency preparedness are available [1,3,6].

The role of hyaluronidase in ocular complications remains particularly uncertain. While hyaluronidase is central to the management of cutaneous vascular compromise caused by hyaluronic acid fillers, its efficacy in established filler-induced visual loss remains uncertain. This distinction is

critical, because reliance on hyaluronidase as a rescue strategy may create a false sense of security when injecting high-risk facial regions. Prevention, anatomical knowledge, early recognition, and urgent ophthalmologic referral remain the most important measures in vision-threatening complications [19,20].

Finally, medicolegal and access-related controversies remain clinically relevant. Any clinician performing hyaluronic acid filler injections should have immediate access to hyaluronidase and be familiar with its preparation, indications, dosing principles, and emergency use. Nevertheless, regulatory restrictions, prescription requirements, cost, training variability, and lack of standardized protocols may limit real-world availability. These barriers reinforce the need for formal training, written emergency protocols, and careful documentation in aesthetic practice [4-6].

Practical Algorithm for Plastic Surgeons

A practical approach to hyaluronidase use should begin with classification of the clinical scenario as elective correction, suspected inflammatory complication, or emergency vascular compromise.

For elective correction, such as overfilling, asymmetry, Tyndall effect, superficial deposits, migration, or persistent edema, the surgeon should perform a careful clinical assessment, review the type and timing of filler used, document baseline findings, and consider ultrasound when the filler location is unclear. Conservative, targeted hyaluronidase administration is preferred, followed by reassessment before additional treatment [1,3,16].

For nodules or delayed inflammatory reactions, the surgeon should avoid assuming that all nodules are simple filler accumulations. Evaluation should consider infection, biofilm, granulomatous reaction, delayed immune-mediated inflammation, or non-hyaluronic acid products. Hyaluronidase may be appropriate when hyaluronic acid filler is suspected or confirmed, but additional treatment such as antibiotics, anti-inflammatory therapy, drainage, or biopsy may be required depending on clinical findings [2,3].

For suspected vascular occlusion, treatment should be immediate. The injection procedure should be stopped, perfusion should be assessed, and hyaluronidase should be administered promptly into the affected region and along the suspected vascular territory. Repeat dosing should be performed according to clinical response, including improvement in pain, color, capillary refill, and tissue perfusion. Adjunctive measures such as warming, gentle massage, analgesia, and close follow-up may be considered, but they should not replace hyaluronidase administration [1,4,5].

When ultrasound is available and can be performed without delaying treatment, it may help identify filler deposits, evaluate vascular compromise, guide targeted hyaluronidase injection, and document restoration of flow. In complex cases

or impending necrosis, ultrasound-guided treatment may improve precision and potentially reduce unnecessary enzyme use [16-18]. However, in a clinically obvious emergency, the absence of ultrasound should not delay treatment [4,5].

For ocular symptoms, the event should be treated as a medical emergency. The procedure must be stopped immediately, and urgent ophthalmologic evaluation should be activated. Hyaluronidase may be considered as part of local protocols, but the surgeon must recognize that evidence for visual recovery is limited and that prevention remains the most important strategy [1-3].

Medicolegal and Ethical Considerations

The medicolegal relevance of hyaluronidase in aesthetic plastic surgery is substantial. Because vascular occlusion is a known complication of hyaluronic acid filler injection, clinicians who perform filler procedures should have immediate access to hyaluronidase, understand its indications, and be trained in emergency management. Lack of access to hyaluronidase or inability to recognize vascular compromise may increase the risk of preventable harm and medicolegal exposure [4-6].

Informed consent should explicitly mention the possibility of filler-related complications, including vascular occlusion, skin necrosis, scarring, infection, inflammatory reactions, asymmetry, need for reversal with hyaluronidase, and rare vision-threatening events. Patients should also understand that hyaluronidase may dissolve the intended aesthetic result and may require additional procedures or staged correction [1,3].

Documentation is essential. The medical record should include the filler product, lot number, injection site, amount injected, plane of injection, technique, needle or cannula type, immediate patient response, and any complication-management steps. When hyaluronidase is used, the dose, dilution, anatomical location, timing, number of administrations, clinical response, photographs, and follow-up findings should be recorded [4-6].

Ethically, clinicians should avoid performing filler injections without adequate complication preparedness. This includes having hyaluronidase available, maintaining emergency protocols, recognizing early signs of ischemia, and referring promptly when ocular or severe vascular symptoms occur. In aesthetic practice, patient safety must take priority over preservation of the cosmetic result.

Discussion

Hyaluronidase occupies a unique position in aesthetic plastic surgery because it is both a corrective tool and an emergency rescue agent. The increasing use of hyaluronic acid fillers has made hyaluronidase an essential component of complication management, particularly because hyaluronic acid remains the only commonly used filler material with a clinically available enzymatic reversal option. However, the concept of

reversibility should be interpreted cautiously. Although hyaluronidase can effectively degrade hyaluronic acid filler deposits, its clinical success depends on early recognition of complications, appropriate dosing, correct anatomical delivery, filler characteristics, and the severity of the adverse event [1-4,11].

A central finding of the current literature is that hyaluronidase use differs substantially between elective and emergency settings. In elective scenarios, such as overcorrection, asymmetry, Tyndall effect, filler migration, or persistent edema, the goal is controlled correction. Conservative and targeted administration is usually preferable to avoid excessive volume loss or contour irregularities [1,3,6]. In contrast, suspected vascular occlusion requires immediate and decisive treatment, as delayed intervention can result in tissue necrosis, scarring, and permanent aesthetic or functional sequelae [4,5]. This distinction is clinically important because protocols designed for elective correction should not be extrapolated to ischemic emergencies.

Dosing remains one of the most important unresolved issues. Available evidence demonstrates that different hyaluronic acid fillers do not respond uniformly to hyaluronidase. Their degradation depends on concentration, cross-linking technology, cohesivity, rheologic profile, and tissue integration [7-15]. These findings challenge the use of a single universal dose for all clinical situations. Instead, dosing should be individualized according to the indication, severity of presentation, anatomical site, suspected filler type, and clinical response. In emergency vascular compromise, repeated dosing may be necessary until objective improvement in pain, color, capillary refill, and tissue perfusion is observed [1,4,5].

Ultrasound-guided hyaluronidase represents an important advance in the management of filler complications. By allowing visualization of filler deposits, vascular structures, and Doppler flow, ultrasound may improve diagnostic accuracy and enable more precise enzyme delivery [16-18]. This is particularly valuable in complex cases, deep filler deposits, persistent edema, migration, nodules, and vascular compromise. Nevertheless, ultrasound should be considered an adjunct rather than a prerequisite in urgent ischemic scenarios. When vascular occlusion is clinically suspected and ultrasound is not immediately available, treatment should not be delayed [4,5,17,18].

Ocular complications represent the most severe and controversial scenario. Unlike cutaneous vascular occlusion, where hyaluronidase has a well-established role, its efficacy in established filler-induced visual loss remains uncertain. Reports have described periocular, retrobulbar, orbital, and intra-arterial approaches, but visual recovery remains inconsistent and often poor [19,20]. This distinction is essential for plastic surgeons: hyaluronidase should not create a false sense of safety when injecting high-risk regions such as the nose, glabella, forehead, temple, and upper midface. Prevention, anatomical knowledge, conservative injection

technique, immediate recognition of visual symptoms, and urgent ophthalmologic referral remain the most important measures [19,20].

Safety considerations also influence clinical decision-making. Hyaluronidase is generally well tolerated, but local reactions and rare hypersensitivity events can occur [1-4,11]. Skin testing remains controversial. It may be considered in selected elective cases, especially when there is a history suggestive of hypersensitivity, but it should not delay treatment in suspected vascular occlusion. In emergency settings, the risk of irreversible tissue injury generally outweighs the theoretical risk of allergic reaction, provided that the clinician is prepared to recognize and manage hypersensitivity appropriately [1,3,6].

The current evidence base has several limitations. Much of the available literature consists of narrative reviews, scoping reviews, in vitro studies, case reports, small case series, and expert-based recommendations. Although these studies provide valuable guidance, high-quality prospective data remain limited. In vitro degradation studies are useful for understanding filler behavior but may not fully reproduce clinical conditions, where tissue integration, vascular anatomy, timing, inflammation, and injection technique influence outcomes [7-15]. Similarly, evidence supporting ultrasound-guided hyaluronidase is promising but still evolving, and larger comparative studies are needed to determine whether it improves outcomes compared with conventional techniques [16-18].

Overall, the available evidence supports a severity-based approach. Elective correction should be conservative, targeted, and reassessed over time. Suspected vascular occlusion should be treated immediately with adequate and repeated hyaluronidase administration as needed. Ultrasound guidance should be used when available and when it does not delay urgent care. Ocular symptoms should prompt immediate emergency referral, because the role of hyaluronidase in established visual loss remains unproven. For plastic surgeons, optimal hyaluronidase use requires not only technical familiarity with the enzyme but also preparedness, documentation, patient counseling, and structured complication protocols [1,3-6,19,20].

Future Directions

Future research should focus on standardizing hyaluronidase protocols according to indication, anatomical region, filler type, severity of complication, and availability of ultrasound guidance. Current evidence demonstrates variability in filler responsiveness and dose-dependent degradation, but clinical protocols remain heterogeneous [7-15].

Prospective studies comparing low-dose, high-dose, and repeated-dose protocols are needed, particularly in vascular occlusion and impending skin necrosis. Additional studies should also evaluate whether ultrasound-guided hyaluronidase improves outcomes compared with conventional flooding techniques, reduces total enzyme dose,

shortens recovery time, or decreases the risk of tissue loss [16-18].

Another important area is formulation-specific research. Comparative studies between ovine-derived and recombinant human hyaluronidase suggest differences in degradation behavior, but further clinical data are needed to determine whether these differences translate into meaningful outcome advantages [8,12].

Training and credentialing also require attention. Plastic surgeons and aesthetic injectors should be trained not only in filler placement but also in complication recognition, vascular anatomy, ultrasound use, hyaluronidase preparation, emergency dosing, and medicolegal documentation. Multicenter registries of filler complications may help define best practices and reduce variability in care [4-6].

Finally, ocular complications require stronger evidence. The role of hyaluronidase in filler-induced visual loss remains uncertain, and future studies should clarify whether any route, timing, or protocol can meaningfully improve visual outcomes. Until then, prevention, early recognition, and immediate ophthalmologic referral remain essential.

Conclusions

Hyaluronidase is an indispensable agent in aesthetic plastic surgery for the management of hyaluronic acid filler-related complications. Its role is well established in elective correction of overfilling, superficial deposits, migration, Tyndall effect, and selected nodular reactions, but its most critical application is the urgent treatment of suspected vascular occlusion. Current evidence supports early and decisive administration when ischemia is suspected, with repeat dosing guided by clinical response [1,3-5].

Despite its importance, hyaluronidase use remains surrounded by significant controversy. Optimal dosing, dilution, timing, injection technique, formulation selection, allergy testing, and ultrasound guidance have not been universally standardized. Furthermore, the response of different hyaluronic acid fillers to hyaluronidase varies, challenging the concept of a single universal protocol [6-15]. Ultrasound-guided hyaluronidase represents a promising advance, particularly for complex filler complications and vascular compromise, but access and training remain limiting factors [16-18]. Plastic surgeons should maintain immediate access to hyaluronidase, understand its limitations, use structured emergency algorithms, and document management carefully. Future studies should focus on standardized protocols, filler-specific dosing, ultrasound-guided treatment outcomes, and the unresolved role of hyaluronidase in vision-threatening complications.

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