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Review

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Management of visual complications of dermal filler injections

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Abstract

Injectable cosmetic fillers have dramatically risen in popularity in recent years. However, as the use of such fillers has become more common, there have been many reports of vision loss secondary to misplaced filler embolizing to the ophthalmic artery, resulting in ocular ischemia. Currently, there are no randomized control trials or widely validated clinical guidelines that dictate how injectors should manage ischemic complications of filler embolism. This review aims to explain the possible mechanisms by which a cosmetic filler embolus can occlude the ophthalmic artery and describe the types of treatments that have been attempted thus far. Additionally, this article uniquely delineates a possible stroke-like protocol that can be implemented in order to restore perfusion and recover vision after such ischemic complications have occurred.

Keywords: Vision loss, complications of fillers, ocular ischemia, stroke, hyaluronic acid, platelet-rich plasma

INTRODUCTION

The use of injectable cosmetic fillers has rapidly become increasingly popular in recent years—dermal fillers now represent the second most common nonsurgical aesthetic procedure[1]. In 2021 alone, consumer spending on injectable cosmetic fillers in the United States amounted to over $1 billion[2]. With this increase in injections comes an increase in retrograde embolism of cosmetic fillers and ophthalmic ischemia[3,4].

Filler emboli have been shown to induce ophthalmic artery occlusion (OAO), central retinal artery occlusion (CRAO), branch retinal artery occlusion (BRAO), and other orbital vascular occlusions[5]. Previous studies have established that permanent retinal damage resulting in vision loss occurs after 90 minutes of non-perfusion, suggesting that timely intervention is key when vascular occlusion occurs[6]. Presently, there is no first-line protocol for rapid reperfusion in ischemic filler complications to reverse the vision changes associated with ocular ischemia. This article will review current proposed reperfusion techniques, and build on previous cases presented in the literature in order to devise possible stroke-like protocols for addressing the ocular ischemic complications of dermal filler injection.

MECHANISM OF OPHTHALMIC COMPLICATIONS OF FILLER INJECTION

The main proposed pathophysiology of ophthalmic injury following injection of cosmetic filler is retrograde embolism through an artery adjacent to the injection site, most commonly the supratrochlear, supraorbital, or dorsal nasal arteries, which are derived from the internal carotid artery [Figure 1]. These arteries also anastomose with the external carotid artery via the ophthalmic artery. The supratrochlear and supraorbital arteries can inadvertently be infiltrated when injecting filler into the glabellar region, while the dorsal nasal artery is more likely to be accessed at the nasolabial fold. When the filler material is injected into one of these distal arteries, the relatively higher pressure of the injection compared to arterial pressure causes the filler to travel proximally towards the internal carotid, where it can embolize to the ophthalmic artery[7,8]. Ischemia occurs due to primary obstruction of blood flow by the embolus itself and secondary triggering of local inflammation, platelet aggregation, and activation of the coagulation cascade. Lastly, larger emboli and clots can break into smaller micro-emboli and lodge in distal branches of the ophthalmic artery, causing multifocal vessel occlusion. The resulting orbital ischemia can be disastrous, causing permanent blindness, ptosis, ophthalmoplegia, anterior segment dysfunction, and ultimately phthisis bulbi as demonstrated by a recent case report of vision loss associated with platelet-rich plasma injections to the forehead[9].

The ischemic consequences of filler-induced embolism can differ depending on the anatomic location affected. If the filler embolus lodges in the central retinal and posterior ciliary arteries, occlusion causes non-perfusion of the retina, manifesting as vision loss that can become permanent once irreversible retinal cell death occurs[8]. Occlusion of the posterior ciliary arteries and anterior ciliary arteries can limit blood flow to the iris and ciliary body, causing anterior segment ischemia, as well[10].

The type of cosmetic filler that is administered can also affect the extent of embolism and the ischemic sequelae that occur. Previously, fillers implicated in reports of visual complications have included hyaluronic acid, platelet-rich plasma (PRP), autologous fat, calcium hydroxyapatite, and periorbital aesthetic poly-(L)-lactic acid (PLLA)[11,12]. Autologous fat has been demonstrated to be more likely to induce a proximal arterial obstruction given its relatively larger particle size. Hyaluronic acid has been thought to occlude more distal branches of the ophthalmic artery due to its smaller particle size and can possibly also block perfusion by drawing water into adjacent soft tissues and thereby reducing the pressure gradient between the ophthalmic artery and its smaller branches. Platelet-rich plasma (PRP) can cause more severe ischemia since it is more pro-thrombotic than other fillers due to its composition-a highly concentrated amalgamation of a patient's own platelets and associated growth factors, 2.5-8 times higher than normal serum concentration[13].

TREATMENT OF OPHTHALMIC FILLER EMBOLISM

In any case of embolic vascular occlusion, treatment requires reestablishing perfusion and oxygenation of the affected tissue. This can be achieved by adjuvant therapies that focus on clot and embolus displacement or increased oxygen tension, thrombolytic therapies that break down fibrin clots, or specific embolism lysis

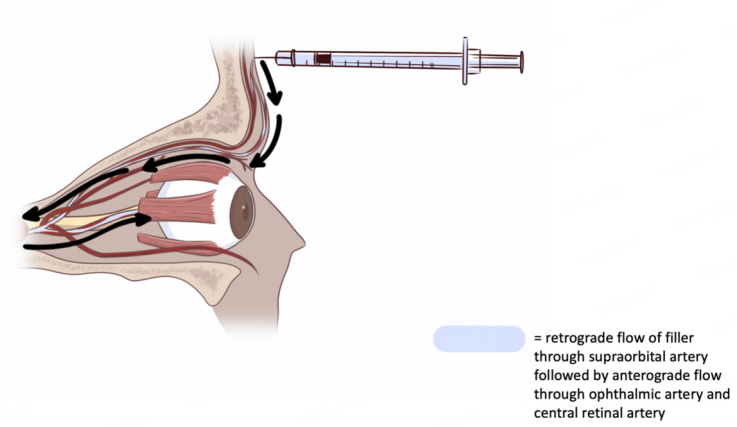

Figure 1. Anatomical diagram depicting retrograde embolism of dermal filler to ophthalmic artery via inadvertent injection of filler directly into supraorbital artery.

agents. None of the therapies described below have demonstrated efficacy from randomized data - this is expected given the current rarity of filler embolism. Even so, they warrant discussion because ischemia requires rapid reperfusion to restore function based on retinal models, and any future trials will depend on rapid treatment protocols similar to those developed in the stroke and cardiovascular literature.

Local administration of reversal agents

Hyaluronic acid is the only cosmetic filler with a specific treatment, hyaluronidase, which facilitates enzymatic degradation of the filler. Previous studies have examined the efficacy of injecting hyaluronidase via subcutaneous, retrobulbar, or intra-arterial approaches in an effort to reverse ischemia[14,15]. Subcutaneously administered hyaluronidase can pass through tissue and diffuse across the arterial wall. A systematic review of 144 cases of using hyaluronidase to manage vision loss associated with hyaluronic-acid injection revealed varying success in improving visual acuity, even when injection occurred immediately after vision loss[16]. However, multiple patients demonstrated visual recovery when hyaluronidase was injected adjacent to the supraorbital or supratrochlear arteries, which have been implicated as possible areas of retrograde embolism of filler, further supporting this theory. Intra-arterial injection of hyaluronidase also resulted in partial visual recovery in multiple patients, suggesting that future research could examine the efficacy of rapid administration either directly into or next to the likely site of retrograde embolism to prevent permanent vision damage. With retrobulbar injection of hyaluronidase, only one patient experienced an improvement in visual acuity, and it was questionable whether her clinical recovery could be attributed to hyaluronidase injection or the resolution of the corneal edema she exhibited at initial presentation. Though there are limited reports of successfully using hyaluronidase to break down displaced hyaluronic acid filler, further research could examine the efficacy of administering hyaluronidase immediately after initial vision loss as well as the utility of devising reversal agents for other types of cosmetic fillers.

Potential use of thrombolytics or antiplatelet medications

Urokinase, tissue plasminogen activator (tPA), and tenecteplase (TNK) are thrombolytic agents that activate plasmin, which breaks down fibrin and fibrinogen, the final common components of the coagulation cascade. Intravenous administration of tPA or TNK is the current mainstay of endogenous stroke management and could be employed to treat iatrogenic ophthalmic artery occlusion following cosmetic filler embolism. Previous studies have revealed that filler-induced clots may induce a higher degree of vasospasm and thrombosis than those produced by endogenous emboli due to a combination of occlusion

by filler embolus and platelets and fibrin that are drawn to the area of occlusion as part of the inflammatory and thrombotic response[17,18].

There are not yet any reported cases of injecting intravenous tPA after retrograde embolism of cosmetic filler, but urokinase has been used in filler embolism and there are various meta-analyses of the utility of tPA in endogenous CRAO. In a meta-analysis of intravenous fibrinolysis for CRAO, Mac Groryof *et al.* examined 67 patients who received tPA less than 4.5 h after CRAO and noted visual recovery in 37.3%, which is higher than the rate of recovery of 17.7% previously noted in patients who did not undergo any therapeutic intervention[19].

Studies investigating the utility of intra-arterial thrombolysis to treat non-iatrogenic CRAO suggest variable efficacy[20]. A systematic meta-analysis published by Page *et al.* revealed an odds ratio of 2.52 with a 95% confidence interval (1.69 - 3.77) that intra-arterial tPA can increase visual recovery after CRAO[21]. Similarly, a meta-analysis by Page *et al.* also indicated that 34.9% of patients who received intra-arterial therapy demonstrated significant improvement in visual acuity[21]. Many such studies are limited in interpretation given the large variability in time to treatment and the fact that many endogenous CRAOs can self-resolve with time. Also, most of these studies focused on visual acuity as a marker of clinical improvement, though additionally assessing visual fields could provide more information about the recovery of perfusion to areas of the retina beyond the fovea.

In terms of intra-arterial thrombolysis in the setting of filler-induced vision loss, a paper by Zhang *et al.* examined the utility of IAT with urokinase in combination with hyaluronidase specifically in patients who experienced vision loss after hyaluronic acid filler embolism[8]. In this paper, 10 out of 24 patients treated with either hyaluronidase or combined hyaluronidase and urokinase experienced improvement in visual acuity. While 36% of the patients who received intra-arterial hyaluronidase exclusively exhibited visual recovery, 46% of patients who received both hyaluronidase and urokinase experienced improvement in visual acuity. In another study, combining hyaluronidase with tPA resulted in 100% of patients having either partial or complete reperfusion, whereas hyaluronidase alone resulted in 60% exhibiting recovery of vision[15]. These findings suggest that intra-arterial thrombolysis with a combination of agents rather than one reversal agent alone could maximize the restoration of vision after filler embolism, though validation via randomized controlled trial is necessary to vet IAT as a viable treatment option.

Table 1 includes a compilation of all reported cases of attempted intra-arterial thrombolysis (IAT) to treat cosmetic filler-related embolism and vision loss. To date, IAT has only been attempted in patients who received fillers composed of hyaluronic acid or fat. For the most part, improvement in visual acuity was generally minimal, though time to treatment was usually several hours after the initial loss of vision, which is well past the time limit for irreversible retinal ischemia and could explain the variable success in instances of IAT after filler-related embolism.

One conceivable concern regarding thrombolysis with tPA is the risk of inducing a hemorrhage or other possible related systemic adverse effects. With regards to intravenous tPA use, previous research has demonstrated that the risk of inducing a hemorrhage by administering intravenous tPA to patients without a confirmed stroke is low. In a large multi-center study of 75,582 patients, the rate of symptomatic intracranial hemorrhage was 3.5% in stroke patients versus 0.4% in stroke mimics[30]. These findings suggest that given the minimal risk of disastrous hemorrhagic effects, clinicians should consider the potential utility of performing intravenous thrombolysis with tPA in filler embolism. Additionally, further research could investigate the safety of intra-arterial tPA via the site of filler injection as a therapeutic option, as this would

Table 1. Recent reports of intra-arterial thrombolysis in the setting of filler embolism

Author	Age (years)	Sex	Material	Pre-treatment visual acuity	Time to treatment after symptom onset (h)	Thrombolytic agent	Visual acuity outcome
Kim *et al.*, 2016[22]	19	Female	Hyaluronic acid	NLP, unilateral	N/A	Hyaluronidase	NLP, unilateral
Chen *et al.*, 2018[23]	20	Female	Hyaluronic acid	Vision loss	2	Hyaluronidase, urokinase	NLP, OD
Oh *et al.*, 2014[24]	33	Female	Hyaluronic acid	NLP, OD	10	Hyaluronidase, urokinase	NLP, OD
Kim *et al.*, 2015[25]	24	Female	Hyaluronic acid	NLP, OD	3.5	Hyaluronidase	NLP, OD
Kim *et al.*, 2015[25]	34	Female	Hyaluronic acid	NLP, OD	5	Hyaluronidase	NLP, OD
Kim *et al.*, 2015[25]	39	Female	Hyaluronic acid	HM, OS	3	Hyaluronidase	NLP, OD
Kim *et al.*, 2015[25]	41	Female	Hyaluronic acid	NLP, OD	4.5	Hyaluronidase	NLP, OD
Kim *et al.*, 2015[25]	40	Female	Fat	NLP, OS	2.5	Urokinase, tirofiban	NLP, OS
Kim *et al.*, 2015[25]	66	Female	Fat	NLP, OS	3	Urokinase	NLP, OS
Kim *et al.*, 2015[25]	40	Female	Fat	NLP, OD	5	Urokinase	NLP, OD
Zhang *et al* ., 2020[8]	N/A	Female	Hyaluronic acid	LP, OD	168	Hyaluronidase, urokinase	HM, OD
Zhang *et al* ., 2020[8]	N/A	Female	Hyaluronic acid	NLP, OS	2	Hyaluronidase, urokinase	LP, OS
Zhang *et al* ., 2020[8]	N/A	Female	Hyaluronic acid	NLP, OS	27	Hyaluronidase, urokinase	NLP, OS
Zhang *et al* ., 2020[8]	N/A	Female	Hyaluronic acid	NLP, OS	17	Hyaluronidase, urokinase	NLP, OS
Zhang *et al* ., 2020[8]	N/A	Female	Hyaluronic acid	LP, OD	6	Hyaluronidase, urokinase	20/200, OD
Zhang *et al* ., 2020[8]	N/A	Female	Hyaluronic acid	NLP, OD	25	Hyaluronidase, urokinase	20/50, OD
Zhang *et al* ., 2020[8]	N/A	Female	Hyaluronic acid	NLP, OS	16	Hyaluronidase, urokinase	20/133, OS
Zhang *et al* ., 2020[8]	N/A	Female	Hyaluronic acid	LP, OS	26	Hyaluronidase, urokinase	20/50, OS
Zhang *et al* ., 2020[8]	N/A	Female	Hyaluronic acid	NLP, OS	51	Hyaluronidase, urokinase	NLP, OS
Zhang *et al* ., 2020[8]	N/A	Female	Hyaluronic acid	NLP, OD	22	Hyaluronidase, urokinase	NLP, OD
Zhang *et al* ., 2020[8]	N/A	Female	Hyaluronic acid	NLP, OS	19	Hyaluronidase, urokinase	NLP, OS
Zhang *et al* ., 2020[8]	N/A	Female	Hyaluronic acid	NLP, OS	46	Hyaluronidase, urokinase	NLP, OS
Zhang *et al* ., 2020[8]	N/A	Male	Hyaluronic acid	NLP, OS	75	Hyaluronidase, urokinase	NLP, OS
Zhang *et al* ., 2020[8]	N/A	Female	Hyaluronic acid	NLP, OS	20.5	Hyaluronidase	NLP, OS
Zhang *et al* ., 2020[8]	N/A	Female	Hyaluronic acid	LP, OS	24	Hyaluronidase	HM, OS
Zhang *et al* ., 2020[8]	N/A	Female	Hyaluronic acid	LP, OS	144	Hyaluronidase	20/40, OS
Zhang *et al* ., 2020[8]	N/A	Female	Hyaluronic acid	NLP, OD	24	Hyaluronidase	20/50, OD
Zhang *et al* ., 2020[8]	N/A	Female	Hyaluronic acid	NLP, OD	24	Hyaluronidase	NLP, OD

Zhang *et al*., 2020[8]	N/A	Female	Hyaluronic acid	NLP, OD	32	Hyaluronidase	NLP, OD
Zhang *et al*., 2020[8]	N/A	Female	Hyaluronic acid	NLP, OD	36	Hyaluronidase	NLP, OD
Zhang *et al*., 2020[8]	N/A	Female	Hyaluronic acid	NLP, OS	100	Hyaluronidase	NLP, OS
Zhang *et al*., 2020[8]	N/A	Female	Hyaluronic acid	NLP, OD	14	Hyaluronidase	LP, OD
Zhang *et al*., 2020[8]	N/A	Female	Hyaluronic acid	NLP, OD	24	Hyaluronidase	NLP, OD
Zhang *et al*., 2020[8]	N/A	Female	Hyaluronic acid	NLP, OS	48	Hyaluronidase	NLP, OS
Zhang *et al*., 2021[26]	61	Female	Hyaluronic acid	Blurred vision, OD	26	Hyaluronidase	Blurred vision, OD
Zhang *et al*., 2021[26]	31	Female	Hyaluronic acid	NLP, OD	4	Hyaluronidase	LP, OD
Zhang *et al*., 2021[26]	31	Female	Hyaluronic acid	Blurred vision, OS	6	Hyaluronidase	Blurred vision, OS
Zhang *et al*., 2021[26]	46	Female	Hyaluronic acid	NLP, OD	5	Hyaluronidase	NLP, OD
Nguyen *et al*., 2022[27]	27	Female	Hyaluronic acid	NLP, OD	4	Hyaluronidase	20/50, OD
Wang *et al*., 2021[28]	18-35	29 females, 1 male	Hyaluronic acid	27 individuals with NLP vision in affected eye, 3 individuals with bare LP in affected eye	20-120	Hyaluronidase	Visual acuity improvement in 9 individuals
Xu *et al*, 2021[29]	24	Female	Hyaluronic acid	NLP, OS	6	Hyaluronidase, papaverine	NLP, OS
Xu *et al*, 2021[29]	24	Female	Hyaluronic acid	NLP, OS	7	Hyaluronidase, papaverine	NLP, OS
Xu *et al*, 2021[29]	35	Female	Hyaluronic acid	NLP, OS	10	Hyaluronidase, papaverine	NLP, OS
Xu *et al*, 2021[29]	29	Female	Hyaluronic acid	NLP, OS	8	Hyaluronidase, papaverine	NLP, OS
Xu *et al*, 2021[29]	19	Female	Hyaluronic acid	LP, OD	2	Hyaluronidase, papaverine	HM, OD
Xu *et al*, 2021[29]	21	Female	Hyaluronic acid	NLP, OS	5	Hyaluronidase, papaverine	NLP, OS
Xu *et al*, 2021[29]	19	Male	Hyaluronic acid	NLP, OS	6	Hyaluronidase, papaverine	LP, OS
Xu *et al*, 2021[29]	35	Female	Hyaluronic acid	NLP, OD	5	Hyaluronidase, papaverine	LP, OD

allow for localized administration of thrombolytic and the complications that have previously limited intra-arterial thrombolysis in stroke are related to intracerebral hemorrhage and vascular injury from endovascular therapy[31].

Other studies also suggest that embolism associated with PRP may be more resistant to recanalization via tPA compared to endogenous emboli because tPA targets and promotes the lysis of fibrin rather than directly targeting the platelets themselves[32]. While antiplatelet agents are a mainstay of endogenous stroke therapy, their benefit is largely limited to the prevention of recurrent stroke[33].

Systemic management and adjuvant therapies

Besides interventions localized to the injection site, multiple systemic and adjuvant therapies have been attempted both in the setting of endogenous and iatrogenic filler-associated central retinal artery occlusion. Many of these therapeutic methods focus on lowering intraocular pressure (IOP) to manipulate the pressure gradient within the eye and shift emboli to more distal vessels and preserve central vision. IOP-lowering

treatments including anterior chamber paracentesis, topical anti-glaucoma drops (including beta-adrenergic blocker, carbonic anhydrase inhibitor, prostaglandin analog, and alpha agonist), and intravenous acetazolamide have been proposed[34]. Intravenous mannitol can also be used to create a larger gradient between ischemic tissue pressure and arterial pressure. The use of sublingual glyceryl trinitrate can similarly help alter the pressure gradient by lowering retinal venous pressure[35]. Lastly, ocular massage has been reported to lower intraocular pressure and potentially dislodge emboli[34].

To target the initial inflammatory response and edematous sequelae of retinal ischemia, high-dose systemic glucocorticoids, such as IV methylprednisolone, can be administered to help manage the consequences of CRAO induced by filler embolism[8]. Finally, in some cases, hyperbaric oxygen therapy has been utilized to enhance oxygen delivery to areas of ischemia within the retina until hypoperfusion resolves[34]. However, none of these methods have been validated as a first-line treatment for either endogenous or iatrogenic CRAO, so future randomized control trials could also help determine what kind of role these adjuvant therapies could play in treating cosmetic filler embolism.

Besides treating complications after they have occurred, management of retinal ischemic complications of dermal filler embolism should also begin with preventative measures by noting anatomical considerations and focusing on injection technique prior to filler administration. Knowledge of specific vessel anatomy and possible vascular anastomoses near injection sites is key for avoiding erroneous injection of filler into vasculature. Previous studies have highlighted the benefit of avoiding percutaneous injection altogether and entering through other sites when possible-for example, Yi *et al*. demonstrated a novel intraoral approach to administering hyaluronic acid filler for deep nasolabial folds in order to avoid accidental injection into dorsal nasal artery resulting in blindness[36]. Additionally, using a cannula size of 25G or greater diameter also carries a lower risk of accidentally piercing an arterial wall while injecting fillers[35]. Injecting smaller volumes (0.1 mL per bolus or less) slowly with minimal pressure could also potentially reduce the chance of forcefully lodging a filler embolus into an artery[35]. However, one cadaveric study demonstrated that even small filler amounts could theoretically block the ophthalmic artery and result in blindness, though this study could not account for the perfusion pressures and intravascular hemodynamics of a live person[7]. Therefore, careful attention to vessel anatomy is of utmost importance in addition to injecting small volumes at lower pressures.

STROKE-LIKE PROTOCOLS

Reversal agents for specific filler materials, revascularization using thrombolysis, and systemic and ocular therapies to promote ocular reperfusion all require early intervention. While the efficacy of these therapies has yet to be shown in randomized trials, the need for rapid assessment, early intervention, and post-treatment monitoring suggests that visual complications of cosmetic filler injection should be approached with a stroke-like protocol.

One of the main determinants of resolution of visual impairment is timely intervention-in animal models, rectifying retinal damage has been shown to be possible if blood flow is restored in less than 90 min. After 100 min, there is variability in the amount of retinal recovery and once 4 hours have passed, non-perfusion of the retina results in profound, irreversible infarction[37]. As soon as vision loss and any other focal neurological deficits are noted after injection of cosmetic filler, patients should be referred to a stroke center capable of further neurologic and ophthalmic evaluation and possible revascularization if deemed necessary. Similar to a regular stroke work-up, patients should urgently undergo head computed tomography without contrast to rule out intracranial hemorrhage and head computed tomography with angiography to assess for specific vascular occlusions amenable to thrombectomy. If no alternative diagnoses are identified,

revascularization can be attempted with systemic therapies and reversal agents specific to the type of filler used. If no contraindications to thrombolysis are identified, intravenous tPA could be administered to promote fibrinolysis.

CONCLUSIONS

Over the years, the administration of cosmetic fillers with compositions including hyaluronic acid, fat, and platelet-rich plasma has risen significantly in popularity. Concurrently, there has been an increase in the number of cases of visual complications following filler administration. Protocols for assessing and treating ophthalmic filler emboli must take into account the need for emergent reperfusion in order to salvage tissue. Though there are no proven therapies for cosmetic filler emboli, we believe that treatment should include emergent referral to a stroke center, neurologic and ophthalmologic assessment, non-contrasted and contrasted head imaging, and possible revascularization using reversal agents and adjuvant therapies. Protocolized care will not only improve treatment times, but also support further research on the efficacy of specific therapies.

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Author's contributions

All made substantial contributions to the conception, design, and production of the paper: Madala S, Li J, Gluckstein J, Zhang-Nunes S

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Consent for publication

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REFERENCES

1. Akinbiyi T, Othman S, Familusi O, Calvert C, Card EB, Percec I. Better results in facial rejuvenation with fillers. *Plast Reconstr Surg Glob Open* 2020;8:e2763. DOI PubMed PMC
2. The aesthetic society. Available from: https://cdn.theaestheticsociety.org/media/statistics/2021-TheAestheticSocietyStatistics.pdf [Last accessed on 27 Feb 2024].
3. Rauso R, Sesenna E, Fragola R, Zerbinati N, Nicoletti GF, Tartaro G. Skin necrosis and vision loss or impairment after facial filler injection. *J Craniofac Surg* 2020;31:2289-93. DOI PubMed
4. Mehta P, Kaplan JB, Zhang-nunes S. Ischemic complications of dermal fillers. *Plast Aesthet Res* 2022;9:57. DOI
5. Rohrich RJ, Bartlett EL, Dayan E. Practical approach and safety of hyaluronic acid fillers. *Plast Reconstr Surg Glob Open* 2019;7:e2172. DOI PubMed PMC
6. Hayreh SS, Kolder HE, Weingeist TA. Central retinal artery occlusion and retinal tolerance time. *Ophthalmology* 1980;87:75-8. DOI PubMed

7. Yi KH, Lee HJ, Kim WR, et al. Does injecting small amounts of fillers prevent the development of secondary blindness? *J Cosmet Dermatol* 2024;23:84-9. DOI
8. Zhang LX, Lai LY, Zhou GW, et al. Evaluation of intraarterial thrombolysis in treatment of cosmetic facial filler-related ophthalmic artery occlusion. *Plast Reconstr Surg* 2020;145:42e-50e. DOI
9. Madala S, Bao YK, Lee JH, Gluckstein J, Chang J, Zhang-nunes S. Phthisical eye and orbital ischemia after cosmetic platelet-rich plasma injection to the forehead. *American Am J Ophthalmol Case Rep* 2023;Online ahead of print:101968. DOI
10. Borruat FX, Bogousslavsky J, Uffer S, Klainguti G, Schatz NJ. Orbital infarction syndrome. *Ophthalmology* 1993;100:562-8. DOI PubMed
11. Oh DJ, Jiang Y, Mieler WF. Ophthalmic artery occlusion and subsequent retinal fibrosis from a calcium hydroxylapatite filler injection. *J Vitreoretin Dis* 2019;3:190-3. DOI PubMed PMC
12. Roberts SA, Arthurs BP. Severe visual loss and orbital infarction following periorbital aesthetic poly-(L)-lactic acid (PLLA) injection. *Ophthalmic Plast Reconstr Surg* 2012;28:e68-70. DOI PubMed
13. Kang RS, Seth R, Lee MK, Keller GS. Platelet-rich plasma in cosmetic surgery. *Otolaryng Clin* 2013;5:24-8. DOI
14. Kim DW, Yoon ES, Ji YH, Park SH, Lee BI, Dhong ES. Vascular complications of hyaluronic acid fillers and the role of hyaluronidase in management. *J Plast Reconstr Aesthet Surg* 2011;64:1590-5. DOI PubMed
15. Borzabadi-Farahani A, Mosahebi A, Zargaran D. A scoping review of hyaluronidase use in managing the complications of aesthetic interventions. *Aesthetic Plast Surg* 2022;Online ahead of print. DOI PubMed
16. Xiao H, Kou W, Yang Y, et al. Administration method and potential efficacy of hyaluronidase for hyaluronic acid filler-related vision loss: a systematic review. *Aesthetic Plast Surg* 2022;Online ahead of print. DOI PubMed
17. Baley-Spindel I, Villaseñor-Villalpando E, Márquez-Espriella C, Rivera-Salgado MI, Dávila-Díaz R. Perivascular hyaluronidase with alteplase as treatment for hyaluronic acid thrombosis. *Aesthet Surg J* 2020;40:551-9. DOI PubMed
18. Stark K, Massberg S. Interplay between inflammation and thrombosis in cardiovascular pathology. *Nat Rev Cardiol* 2021;18:666-82. DOI PubMed PMC
19. Mac Grory B, Nackenoff A, Poli S, et al. Intravenous fibrinolysis for central retinal artery occlusion: a cohort study and updated patient-level meta-analysis. *Stroke* 2020;51:2018-25. DOI
20. Hakim N, Hakim J. Intra-arterial thrombolysis for central retinal artery occlusion. *Clin Ophthalmol* 2019;13:2489-509. DOI PubMed PMC
21. Page PS, Khattar NK, White AC, et al. Intra-arterial thrombolysis for acute central retinal artery occlusion: a systematic review and meta-analysis. *Front Neurol* 2018;9:76. DOI PubMed PMC
22. Kim A, Kim SH, Kim HJ, Yang HK, Hwang JM, Kim JS. Ophthalmoplegia as a complication of cosmetic facial filler injection. *Acta Ophthalmol* 2016;94:e377-9. DOI PubMed
23. Chen YC, Wu HM, Chen SJ, et al. Intra-arterial thrombolytic therapy is not a therapeutic option for filler-related central retinal artery occlusion. *Facial Plast Surg* 2018;34:325-9. DOI
24. Oh BL, Jung C, Park KH, Hong YJ, Woo SJ. Therapeutic intra-arterial hyaluronidase infusion for ophthalmic artery occlusion following cosmetic facial filler (hyaluronic acid) injection. *Neuroophthalmology* 2014;38:39-43. DOI PubMed PMC
25. Kim YK, Jung C, Woo SJ, Park KH. Cerebral angiographic findings of cosmetic facial filler-related ophthalmic and retinal artery occlusion. *J Korean Med Sci* 2015;30:1847-55. DOI PubMed PMC
26. Zhang L, Luo Z, Li J, et al. Endovascular hyaluronidase application through superselective angiography to rescue blindness caused by hyaluronic acid injection. *Aesthet Surg J* 2021;41:344-55. DOI
27. Nguyen HH, Tran HTT, Duong QH, Nguyen MD, Dao HX, Le DT. Significant vision recovery from filler-induced complete blindness with combined intra-arterial injection of hyaluronidase and thrombolytic agents. *Aesthetic Plast Surg* 2022;46:907-11. DOI PubMed
28. Wang J, Shen H, Liu T, Li Q, Lyu Z, Yu Y. An efficacy and safety study of intra-arterial recanalization of occluded ophthalmic arteries in patients with monocular blindness caused by injection of hyaluronic acid in facial tissues. *Aesthetic Plast Surg* 2021;45:1573-8. DOI
29. Xu X, Zhou G, Fu Q, et al. Efficacy of intra-arterial thrombolytic therapy for vision loss resulting from hyaluronic acid filler embolization. *J Cosmet Dermatol* 2021;20:3205-12. DOI PubMed PMC
30. Ali-Ahmed F, Federspiel JJ, Liang L, et al. Intravenous tissue plasminogen activator in stroke mimics. *Circ Cardiovasc Qual Outcomes* 2019;12:e005609. DOI PubMed PMC
31. Lee M, Hong KS, Saver JL. Efficacy of intra-arterial fibrinolysis for acute ischemic stroke: meta-analysis of randomized controlled trials. *Stroke* 2010;41:932-7. DOI
32. Tomkins AJ, Schleicher N, Murtha L, et al. Platelet rich clots are resistant to lysis by thrombolytic therapy in a rat model of embolic stroke. *Exp Transl Stroke Med* 2015;7:2. DOI PubMed PMC
33. Minhas JS, Chithiramohan T, Wang X, et al. Oral antiplatelet therapy for acute ischaemic stroke. *Cochrane Database Syst Rev* 2022;1:CD000029. DOI PubMed PMC
34. Cugati S, Varma DD, Chen CS, Lee AW. Treatment options for central retinal artery occlusion. *Curr Treat Options Neurol* 2013;15:63-77. DOI PubMed PMC
35. Humzah MD, Ataullah S, Chiang C, Malhotra R, Goldberg R. The treatment of hyaluronic acid aesthetic interventional induced visual loss (AIIVL): A consensus on practical guidance. *J Cosmet Dermatol* 2019;18:71-6. DOI PubMed PMC
36. Yi KH, Lee JJ, Hur HW, Bae H, Kim HJ. Hyaluronic acid filler injection for deep nasolabial folds: A novel intraoral approach. *Clin*

Anat 2022;35:820-3. DOI PubMed

37. Hayreh SS, Weingeist TA. Experimental occlusion of the central artery of the retina. IV: Retinal tolerance time to acute ischaemia. *Br J Ophthalmol* 1980;64:818-25. DOI PubMed PMC