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Guide for Managing Vascular Occlusion Due to Fillers with Extended Neuro-Ophthalmic Involvement: A Review of Diagnosis, Classification and Treatment

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Abstract

Introduction Filler-induced ophthalmic vascular occlusion (FIVO) is rare but devastating, while stroke remains even less frequent. Hyaluronic acid (HA) accounts for most reported cases of blindness. Given the emergency nature of these events, rapid recognition and immediate preparedness are paramount.

Methods A systematic search of PubMed, Web of Science, and the Cochrane Library was conducted up to August 2025 in accordance with PRISMA 2020 guidelines. Studies addressing vascular occlusion with neuro-ophthalmic involvement from dermal fillers, including technical and pharmacological management, were reviewed. After screening 48 records, 35 articles met inclusion criteria. Expert consensus statements and recommendations from international panels were also incorporated.

Results Three thematic domains emerged: etiology, classification, and management. Embolic events occur immediately via direct intra-arterial injection or later through embolus fragmentation, migration, or arteriovenous shunting. Temporal classification distinguishes fulminant, immediate, and delayed presentations with distinct prognostic implications. Ophthalmic involvement typically manifests as vision loss, ptosis, or ophthalmoplegia, while neurological complications, including stroke, occur in up to 24% of cases, often affecting the middle cerebral artery. Imaging provides critical diagnostic and therapeutic guidance. Hyaluronidase (HYAL) remains the only intervention consistently associated with improved outcomes, though the optimal delivery route (extraorbital, peribulbar, retrobulbar) remains debated. Adjunctive measures include intraocular pressure reduction, ocular massage, antiplatelet therapy, and hyperbaric oxygen.

Conclusion FIVO is a time-critical emergency. Early intervention with HYAL and supportive measures at the point of care, followed by rapid referral for advanced ophthalmic and neurological evaluation, is essential. Standardized guidelines are urgently needed to harmonize practice and improve patient outcomes.

Level of Evidence V This journal requires that authors assign a level of evidence to each submission to which Evidence-Based Medicine rankings are applicable. This excludes Review Articles, Book Reviews, and manuscripts that concern Basic Science, Animal Studies, Cadaver Studies, and Experimental Studies. For a full description of these Evidence-Based Medicine ratings, please refer to the Table of Contents or the online Instructions to Authors www.springer.com/00266.

Keywords Dermal fillers · Vascular occlusion · Blindness · Stroke · Hyaluronic acid · Complications

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Introduction

Vascular complications from fillers have a relatively low incidence, with one vascular complication occurring for every 5000 vials [1]. Ophthalmic involvement is an even rarer complication with significant clinical implications, while the incidence of stroke remains very low. The product most frequently associated with blindness is hyaluronic acid (HA), accounting for 70% of cases [2]. The anatomical area most prone to neuro-ophthalmic embolism is the nose, followed by the forehead, with the glabella ranking third, significantly lower than the others [2, 3].

Given that complications are bound to occur and often present as medical emergencies, the only effective strategy is preparation. First and foremost, it is essential to have the appropriate resources and medication readily available to manage such incidents [4]. Once we are equipped with the necessary tools to address neuro-ophthalmic complications, the next critical step is early diagnosis and treatment.

This study reviews the latest data on vascular complications management caused by dermal fillers focusing on the extended neuro-ophthalmic involvement. It examines the underlying etiology of embolism, the temporal classification of neuro-ophthalmic complications, and the clinical spectrum of ophthalmic and neurological manifestations. Diagnostic strategies, including imaging, are outlined alongside current therapeutic approaches, with emphasis on timely interventions and the integration of ophthalmic and neurological management to optimize outcomes.

Methods

A systematic literature review was conducted using PubMed, Web of Science, and the Cochrane Library, under the assumption that articles not indexed in these databases may lack sufficient scientific rigor for inclusion. No external funding was received for this study. The search included publications up to January 2026. The selection criteria encompassed all key aspects of vascular occlusion management related to neuro-ophthalmic complications caused by dermal fillers, addressing both technical and pharmacological considerations, while excluding studies focused exclusively on cutaneous involvement.

Following the initial selection, additional articles with significant clinical relevance, as determined by the investigators, were also included. All relevant neuro-ophthalmic reviews and clinical case reports were considered. Animal studies, experimental studies, purely technical reports, and product-focused investigations were excluded. This comprehensive literature review also integrated insights from international leaders and recommendations from expert panels.

The keywords used were "Dermal Fillers," "Vascular Occlusion," "Complications," "Blindness," and "Stroke," yielding a total of 60 records. The methodology was conducted in accordance with the PRISMA 2020 guidelines (Fig. 1). After removal of 12 duplicate citations, 48 records remained for screening. All 48 were screened and evaluated for eligibility. Thirteen articles were excluded, including 3 animal studies, 4 anatomical or histopathological studies, 2 technical reports, and 4 studies deemed not directly relevant (e.g., general safety or unrelated focus). Ultimately, 35 articles met the inclusion criteria and were incorporated into the final analysis. These included 23 review articles, one of which was a meta-analysis, and 12 clinical case reports, of which three were case series.

The objective of this review was to develop a clear, practice-oriented guide for the management of vascular occlusion with neuro-ophthalmic involvement. Specifically, the aims were to classify neuro-ophthalmic vascular injuries to enable consistent future data analysis and facilitate comparison between patients, and to support clinical decision-making in neuro-ophthalmic emergencies, including both blindness and stroke. The review also aimed to assist in early recognition, severity stratification, and appropriate escalation of care to guide tailored clinical management. Given the heterogeneity of the available literature and the absence of comprehensive standardized guidelines, a narrative review format was selected to synthesize the most clinically relevant aspects of each article.

Results

The following revision is based on the current evidence on filler-induced embolic complications across key themes. It reviews the etiology and mechanisms of vascular and neuro-ophthalmic embolism, followed by the temporal neuro-ophthalmic classification for prognosis and treatment guidance. Ophthalmic and neurological involvement are summarized in terms of clinical presentation, diagnosis, and stroke classification. The importance of imaging for vascular assessment and an overview of therapeutic strategies for both ophthalmic and neurological management are also discussed.

Etiology of Embolism

Neuro-ophthalmic involvement can occur immediately following direct embolization from a vascular injection site or later, after the administration of hyaluronidase (HYAL) [5], with subsequent fragmentation of the intravascular embolus or secondary to vasodilation. There have also been

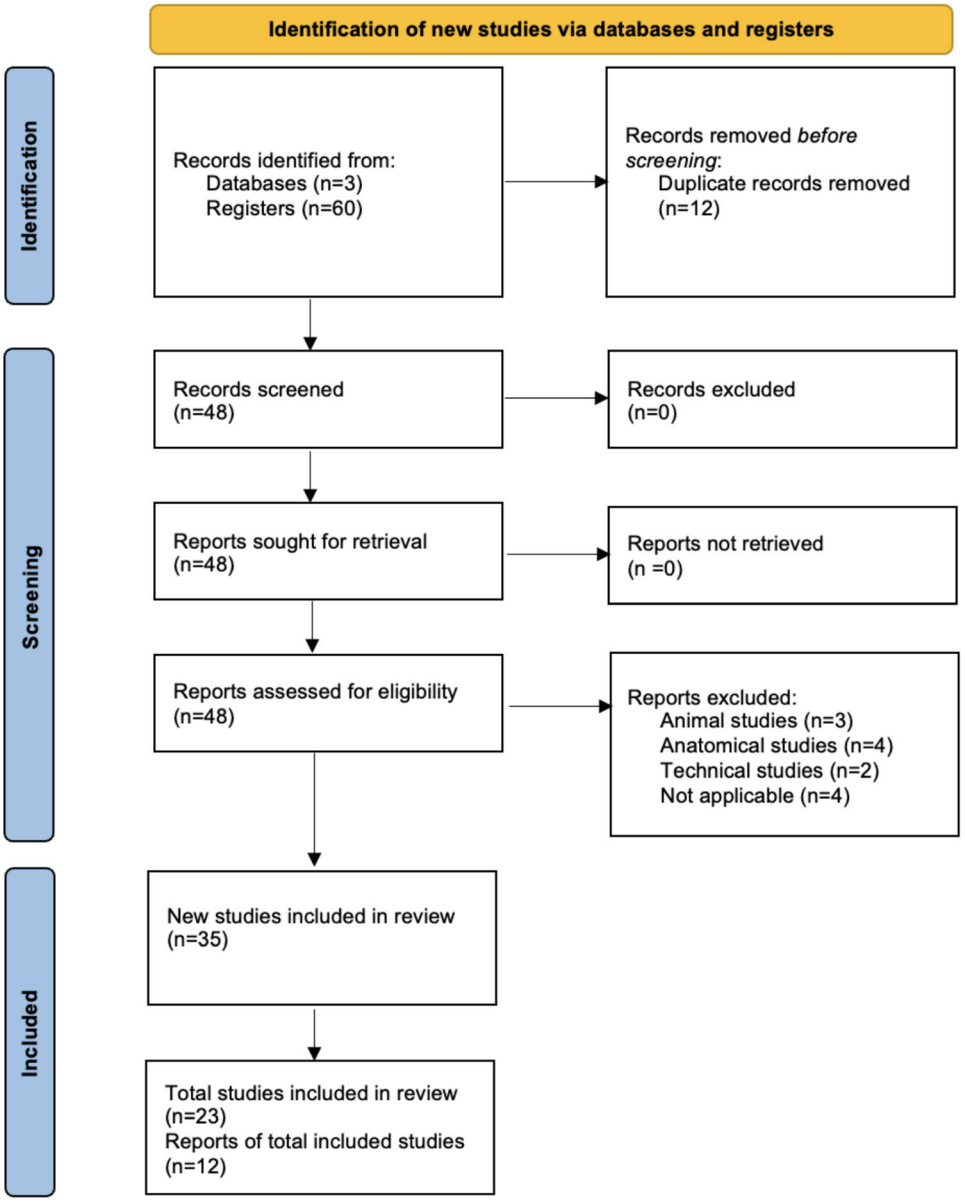

Fig. 1 PRISMA 2020 flow diagram

reported cases of delayed onset from a venous vascular area, where, through arteriovenous shunts such as the patent foramen ovale [3], or those present in the pulmonary branches, the embolus can migrate to the arterial circulation. Additionally, facial venous-arterial shunts [6] have been described, which may lead to delayed neuro-ophthalmic embolism.

Wang et al. [3] proposed a list of possible vascular conditions: arterial involvement with soft tissue damage, ocular involvement, stroke, and facial paralysis. On the venous side, local thrombophlebitis, cerebral venous sinus thrombosis, or migration to the lungs causing pulmonary embolism can occur. In the presence of shunts, distant arterial vascular embolism may also develop.

The chronology of various embolic lesions caused by fillers requires continuous reevaluation of the patient, both before and after the administration of HYAL. It is also important to suspect the presence of embolic disease in the medium to short term in patients without cardiovascular risk factors who have a history of biocompatible HA implants.

Neuro-Ophthalmic Temporal Classification

In the temporal classification of blindness due to fillers following injection, we can distinguish three main types, which are also extended to neurological involvement. One or more embolization mechanisms may coexist and may

appear progressively in several phases. For instance, immediate ophthalmic involvement may occur with delayed or late neurological involvement.

Type I, or immediate onset, occurs within the first hour after treatment and most commonly within the first 10 min, which represents the highest-risk period. Tamura et al. reported an incidence of 79.6% for this time window [7], while data from the FDA panel showed a similar incidence of 58% [8]. After the first 10 min, other factors such as mechanical or chemical fragmentation or changes in the angiosome may play a role in determining the progression. Type II occurs within the first 24 hours due to delayed migration of the embolus, with an incidence of 20% [8], while Type III appears beyond 24 hours, with incidences of 9% [8] in the days or weeks following, secondary to arteriovenous communications [6].

The authors propose subdividing Type I into two subtypes. Type IA ("fulminant") refers to events occurring within the first 10 min and is attributed to direct vascular cannulation and immediate embolization. Type IB ("immediate") encompasses events arising between 10 min and 1h after filler injection, typically resulting from embolus retention with subsequent release or migration (Table 1).

Ophthalmic Involvement

Clinical Diagnosis

The ophthalmic presentation will depend on the number of affected vessels. The most common clinical signs, in descending order of frequency, are as follows [2]: no light perception, observed in 229 cases (62.7%); ptosis in 205 cases (56.2%); ophthalmoplegia in 161 cases (44.1%); and pain in 114 cases (31.2%). Additional symptoms frequently reported include ophthalmodynia, periocular pain, nasal pain, headache, burning sensation, and stinging.

In the diagnostic evaluation, confrontation testing and pupillary examination are essential, and it is important to document timing and promptly contact the on-call ophthalmologist [9, 10]. Visual loss can be urgently and simply classified into three categories: total blindness, where there is no light perception; limited vision, where only light perception is present; and the ability to see hand movements or better, such as counting fingers.

The degree of ocular involvement is prognostic [11]. Total loss of vision indicates involvement of the central retinal artery (CRA), while partial vision perception suggests occlusion of the branches of the CRA or the presence of collateral circulation. Blurred vision indicates involvement of the posterior ciliary arteries (PCA). Ophthalmoplegia and strabismus arise from the involvement of the muscular branches, as well as other branches responsible for the lacrimal system and orbital fat, which have a better overall prognosis since they are non-neurological tissues with a longer ischemic time, unlike the retina [11]. In a study on the recovery of ophthalmoplegia, 77% of patients achieved complete recovery [12]. However, since most patients remain blind, they may develop residual sensory strabismus [11].

Pain is a symptom that appears with the onset of ischemia and also during its resolution, indicating the restoration of blood flow to the affected tissue. Once ischemia is fully established, the pain tends to subside [13].

The extent of ocular involvement is directly associated with the urgency of initiating treatment. It is known that the retina has a variable ischemic time, ranging from 15 to 90 and up to 240 min, depending on the authors [14–17] and the severity of involvement. The presence of residual vision is related to the oxygen supply to the retina, whether due to partial occlusions or the presence of collateral circulation [18]. Based on ischemic time and residual visual function, the urgency of intervention is classified into three risk categories. Grade 1 (critical period) is defined by the absence of light perception and requires immediate intervention within a critical time window of approximately 15 min. Grade 2 (emergency period) is characterized by preserved light perception and necessitates emergent treatment within up to 90 min. Grade 3 (urgent period) is associated with hand motion perception or better and still warrants urgent intervention, with a therapeutic window of up to 240 min (Table 2).

Table 1 Neuro-ophthalmic temporal classification of filler-induced embolic events [6, 12, 18]

Types	Type IA fulminant	Type IB immediate	Type II delayed	Type III late
Temporality	<10 min	10 min–1h	1h–1 Day	1 day or more
Pathophysiology	Direct embolization through vascular cannulation.	Retained embolus and subsequent release due to fragmentation (massage, HSA) or angiosome opening (vasodilator, local anesthetic).	Shares pathophysiology of Type I + II, but more delayed.	Arteriovenous or venoarterial shunt

For ongoing monitoring of visual function, the Snellen 20/20 chart will be used [19]. A visual acuity of 20/20 indicates that a person can see at 20 feet what an individual with normal vision should see at the same distance. In contrast, a visual acuity of 20/200 means that the person must be at 20 feet to discern what someone with normal vision can see at 200 feet, which defines the threshold for legal blindness. In Europe, the use of 6/6 is more common, as it refers to 6 meters, which is equivalent to 20 feet.

Classification of Blindness and Periocular Complication

The classification recommended by Soares [20], adapted from Myung [21], is crucial for prognosis. However, authors aim to expand this and create a new classification by incorporating visual loss into the assessment (Madero-Fakih Ophthalmic Classification) (Table 3). Visual dysfunction can be categorized into three levels: (A) no light perception, indicating complete visual loss; (B) light perception, where the patient can detect the presence of light but cannot discern shapes or movement; and (C) motion perception, where the patient is able to perceive movement without clear visual detail. In this regard, the classification includes various categories to evaluate blindness and periocular complications (Table 3). The degree of dysfunction is closely associated with prognosis and the presence of collateral circulation. Total blindness (no light perception) typically indicates involvement of the ophthalmic artery (OA) or the central retinal artery (CRA), whereas partial vision loss suggests damage to branches of the CRA. Blurred vision is more commonly associated with involvement of the PCA, both of which are generally associated with a more favorable prognosis. Therefore, the extent and pattern of ocular involvement represent critical prognostic factors [11, 18].

Table 2 Time-sensitive classification of retinal ischemia severity [18]

Grade 1	Grade 2	Grade 3
No light perception	Light perception	Hand motion or better
Critical time	Emergency time	Urgent time
15 min	90 min	240 min

Neurological Involvement

Clinical Diagnosis

When ocular involvement occurs, 24% of cases are accompanied by neurological involvement [22]. Therefore, every patient presenting with visual loss should be evaluated to rule out cerebral ischemia [23]. The most common clinical symptom is altered consciousness, followed by hemiplegia, according to the review by Wang et al. [3]. The most frequent location for embolism was the middle cerebral artery [3]. It is believed that the incidence may be higher than initially suspected [3], as the presence of minor clinical signs such as mood changes and memory alterations could be compatible with lacunar infarcts, which are only diagnosed through imaging tests and should raise suspicion of such complications.

Classification of Stroke

The National Institutes of Health Stroke Scale (NIHSS) is a standardized clinical tool used to quantify stroke severity based on neurological deficits observed during examination (Fig. 2) [24]. It is commonly applied in the acute setting to stratify stroke severity. In cases with an NIHSS score greater than 1, the Bamford classification (Fig. 3) may be used to further categorize ischemic stroke syndromes according to their neurological presentation and presumed vascular territory involvement [25]. This system classifies strokes into four clinical subtypes based on history and physical examination findings prior to neuroimaging, providing useful prognostic information regarding stroke location, infarct size, and expected clinical outcomes.

Table 3 Madero-Fakih ophthalmic classification. Adapted from the Myung classification [21] and incorporates visual loss into the assessment. Categories include: no light perception or total blindness (A), light perception only (B), and hand motion or better (C)

Type of blindness	Clinical involvement	All types
None	No neuro-ophthalmic involvement	None
Type 0	Ptosis +/− Ophthalmoplegia. No blindness.	Type 0
Type I blindness	A or B or C	Types IA, IB, IC
Type II blindness	A or B or C + Ptosis	Types IIA, IIB, IIC
Type III blindness	A or B or C + Ophthalmoplegia	Types IIIA, IIIB, IIIC
Type IV blindness	A or B or C + Ophthalmoplegia + Ptosis	Types IVA, IVB, IVC

National institute of Health Stroke Scale (NIHSS)

Item	Description	Score
1a. Level of Consciousness	Alert, drowsy, stuporous, or coma	0 – 3
1b. LOC Questions	Month and age (correct responses)	0 – 2
1c. LOC Commands	Close eyes and grip hand	0 – 2
2. Best Gaze	Horizontal eye movements	0 – 2
3. Visual Fields	Test vision in both eyes	0 – 3
4. Facial Palsy	Symmetry of facial movements	0 – 3
5a. Motor Arm - Left	Holds arm up for 10 seconds	0 – 4
5b. Motor Arm - Right	Same as 5a	0 – 4
6a. Motor Leg - Left	Holds leg up for 5 seconds	0 – 4
6b. Motor Leg - Right	Same as 6a	0 – 4
7. Limb Ataxia	Finger-to-nose or heel-to-shin test	0 – 2
8. Language	Assess speech and comprehension	0 – 3
9. Dysarthria	Clarity of articulation	0 – 2
10. Extinction and Inattention	Detects bilateral stimuli	0 – 2

Total Score: 0 – 42 points

- **0** = No stroke symptoms
- **1–4** = Minor stroke
- **5–15** = Moderate stroke
- **16–20** = Moderate to severe stroke
- **21–42** = Severe stroke

Fig. 2 National Institute of Health Stroke Scale (NIHSS) [24]

Due to the association of neurological alterations in the context of ocular involvement, Rahman E et al. proposed a classification: FAASS (Filler-Associated Acute Stroke Syndrome) [26], based on the Bamford stroke classification (Fig. 3) [25] and the ophthalmic classification by Myung et al. [21]. For monitoring the progression of stroke, authors propose the use of Modified Rankin Scale (mRS) [27].

Imaging Diagnosis

Arteriography remains the gold standard for vascular diagnosis. Ultrasound is the most accessible non-invasive method with high sensitivity and specificity, though it is operator-dependent. Magnetic resonance angiography can differentiate between acute and chronic occlusions [28].

Ultrasound is also useful in diagnosing CRA occlusion. It is a quick and effective diagnostic tool. The main ultrasound signs of vascular occlusion include the retrobulbar spot sign (RBSS), characterized by a hyperechoic spot corresponding to HA embolus. Color Doppler imaging will show an absence of flow in cases of complete arterial

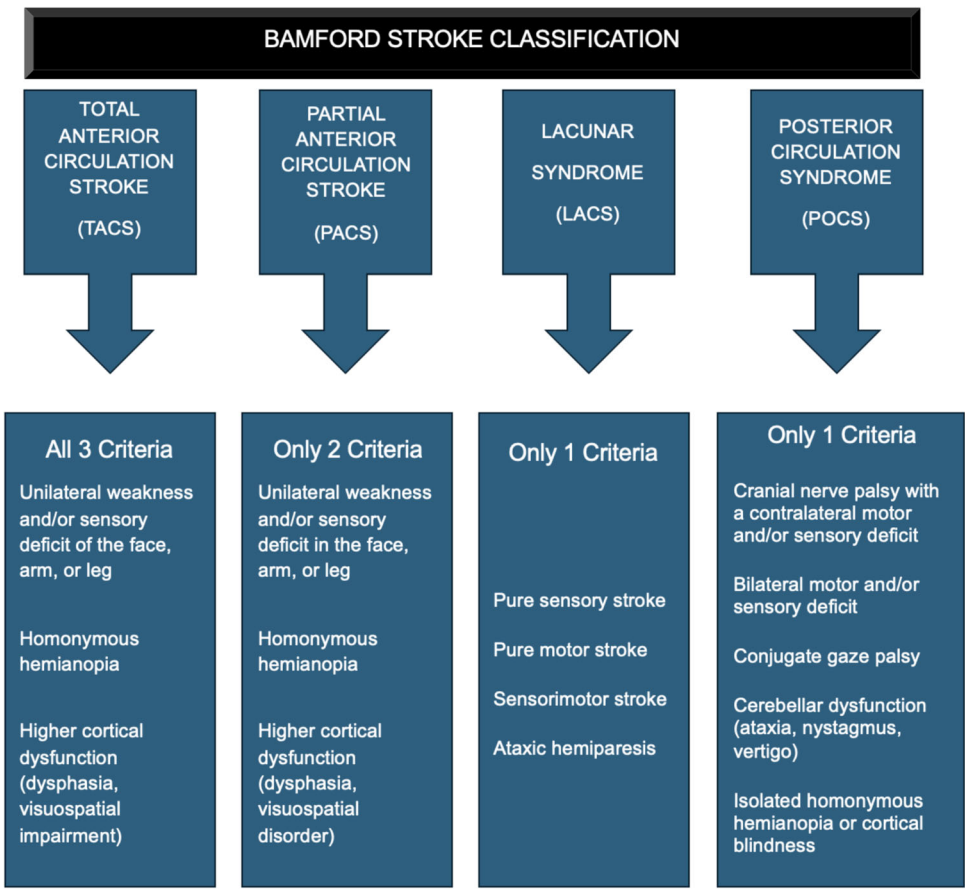

Fig. 3 Bamford stroke classification [25]. *TACS* Total anterior circulation stroke; *PACS* Partial anterior circulation stroke; *LACS* Lacunar stroke; *POCS* Posterior circulation stroke

obstruction. In contrast, stenotic segments may exhibit hypervascularity or accelerated, turbulent flow. Spectral pulsed doppler may reveal either a complete absence of flow or reduced peak systolic velocities and a decreased resistance index [29–31].

Neurological involvement must be diagnosed as quickly as possible in all patients eligible for endovascular treatment through imaging tests. Both non-contrast computed tomography (CT) (Class of Recommendation [COR] I; Level of Evidence [LOE] A; [Table 4]) and magnetic resonance imaging (MRI) (COR I; LOE B-NR) [32] are effective for ruling out intracranial hemorrhage and thereby allowing the initiation of thrombolysis with alteplase. However, CT angiography or MR angiography is recommended in selected patients. These imaging modalities, particularly when combined with diffusion-weighted sequences with or without perfusion, are useful for identifying candidates for thrombectomy within 6 to 24h after the vascular event. In the case of a stroke due to fillers, considering thrombectomy or the supra-selective administration of HYAL, these diagnostic tests would be the preferred choice [32].

Evaluation of Neuro-Ophthalmic Involvement

Given that up to 24% of reported cases present neurological involvement [22] and the clinical impact extends beyond isolated ophthalmic findings, a comprehensive evaluation approach is essential. To enhance diagnostic accuracy and ensure complete neuro-ophthalmic assessment, the authors propose a new integrated evaluation system, the Fakih-Madero Neuro-Ophthalmic Evaluation (Fig. 4). This framework combines detailed ophthalmic assessment using the previously established Madero-Fakih Ophthalmic Classification with a structured neurological evaluation, beginning with the NIHSS to quantify stroke severity [24], followed by the Bamford Stroke Classification to determine the vascular territory and clinical stroke subtype [25], and concluding with neuroimaging to confirm the diagnosis.

Treatment of Neuro-Ophthalmic Complication

Currently, there is no universally standard accepted treatment for neuro-ophthalmic complication caused by fillers [33]. No therapy has been shown to be effective in reversing filler-induced blindness [34]. Stroke management is carried out according to the most recent clinical guidelines [32]. Treatment of the skin and the filler injection site responsible for the embolic event should follow the published recommendations [35]. The management of neuro-ophthalmic complications is divided into two categories: ophthalmic treatment and neurological treatment.

Ophthalmic Treatment

Ophthalmic management of filler-related vascular occlusion carries significant clinical and medicolegal implications [36], and there is currently no standardized consensus regarding the management of vascular occlusion due to dermal fillers with extended neuro-ophthalmic involvement [37–39]. One of the most critical determinants of visual outcome in filler-induced blindness is time, rendering this condition a true medical emergency. Multiple reviews evaluating reperfusion strategies for central retinal artery occlusion (CRAO) consistently emphasize that rapid intervention is the most important factor for salvaging anoxic retinal tissue and improving the likelihood of visual recovery [18].

Intraocular Pressure Reduction (IOPR) (COR I; LOE B) To rapidly lower intraocular pressure (IOP), the patient should be placed in a supine position [37]. Rebreathing into a paper bag has been described as a simple maneuver to transiently lower IOP [40]. This technique increases arterial carbon dioxide levels, which in turn promotes vasodilation of the choroidal and episcleral vessels. The resulting hemodynamic changes can reduce aqueous humor production and facilitate a short-term decrease in IOP. However, the effect is usually modest and short-lived, and the evidence supporting its clinical efficacy remains limited. Moreover, rebreathing should be applied with caution, as prolonged use may lead to systemic complications such as hypoxia or excessive hypercapnia.

Table 4 Consensus-based and GRADE scaling for recommendations

Class of recommendation (COR) (consensus-based)	Level of evidence (LOE) (based on GRADE system)
Level 1 = Strong recommendation "*We recommend…*"	Grade A = High level of evidence
Level 2 = Weak recommendation "*We suggest…*"	Grade B = Moderate level of evidence
Level 3 = Neutral recommendation "*It would be reasonable…*"	Grade C = Low level of evidence
No recommendation	Grade D = Very low level of evidence

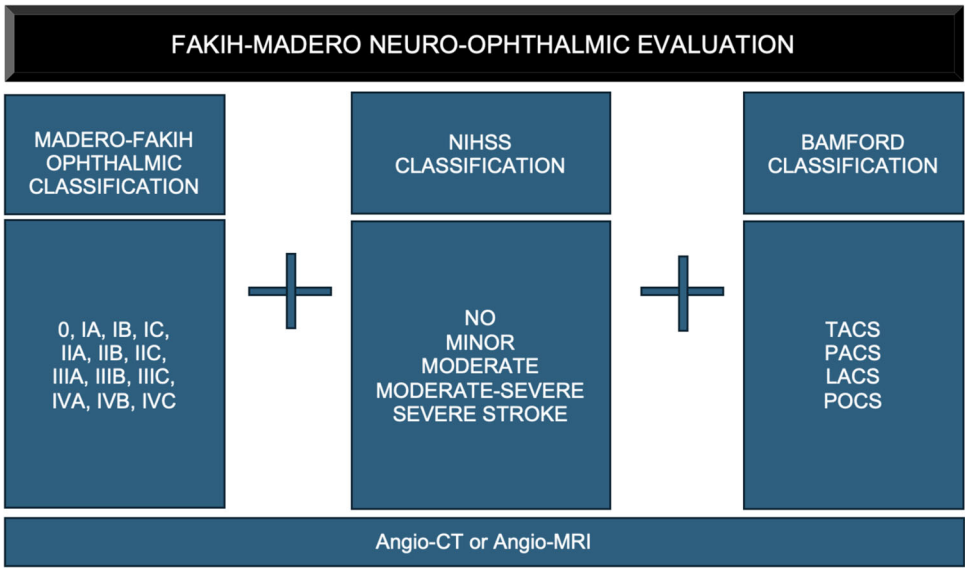

Fig. 4 Fakih-Madero neuro-ophthalmic evaluation. *TACS* Total anterior circulation stroke; *PACS* Partial anterior circulation stroke; *LACS* Lacunar stroke; *POCS* Posterior circulation stroke; *CT* Computed tomography; *MRI* Magnetic resonance imaging

Therefore, this measure is generally considered an adjunctive, temporizing option rather than a definitive treatment for acute intraocular pressure elevation. The most recommended pharmacologic agent for reducing IOP is timolol (COR I; LOE A).

Topical ocular therapy must be administered urgently, and three classes of agents may be used: beta-blockers, carbonic anhydrase inhibitors, and adrenergic stimulants. These drugs have a rapid onset of action, with no evidence demonstrating superiority of one over another [35, 41]. At least two of these agents should be administered as an emergency measure, since combination therapy improves both efficacy and tolerability [41]. There is no consensus on the prevention of acute postoperative IOP elevation; however, alpha-agonists such as brimonidine and apraclonidine are the most frequently used [42]. Additionally, acetazolamide (500 mg every 8h) is recommended to reduce aqueous humor production. Mannitol at 20% (100 ml over 30 min) [37], preferably administered via central line, helps reduce edema and is also beneficial for cerebral edema management (CEM). Anterior chamber paracentesis is recommended by some authors [10, 39].

Anti-Platelet Therapy (APT): (COR I; LOE B) (for HA-Related Thrombosis) Several studies highlight the pro-inflammatory role of intravascular HA, primarily mediated through platelet activation and interactions with leukocytes [43]. HA triggers rapid platelet aggregation, resulting in the formation of a "white thrombus" [37], which further worsens vascular obstruction. Although the exact magnitude of benefit from immediate APT remains uncertain, its use is advocated by drawing parallels with coronary thrombosis, employing an initial loading phase followed by maintenance therapy. This approach is considered essential in the management of filler-induced vascular occlusion [20, 44].

While there is no universally established aspirin (AAS) regimen, a loading dose of 650 mg (commonly in the United States) or 500 mg (Europe and Canada), usually in an enteric-coated form, is often administered, followed by a maintenance dose of 75 mg (USA) or 100 mg (Europe) [44]. According to the updated 2025 American College of Cardiology (ACC)/American Heart Association Joint Committee (AHAJC) guidelines, APT remains unchanged, with AAS administered as a loading dose of 300 mg followed by a maintenance dose of 100 mg [45] (COR I; LOE A; in acute coronary syndrome and acute ischemic stroke) [32, 45].

For patients with hypersensitivity or gastrointestinal intolerance to AAS, clopidogrel (a P2Y12 inhibitor) represents a suitable alternative. Recommended dosing includes a loading dose of 300–600 mg (with 300 mg preferred in cases of fibrinolysis, in individuals older than 75 years, or in those at high hemorrhagic risk), followed by 75 mg daily [35, 46]. APT is generally continued for 15 days (Table 5).

HYAL (COR I; LOE B) Management includes treatment of the site of embolic origin with HYAL, following the 2025 guide for vascular occlusion with cutaneous involvement [35]. This protocol, consistent with the 2021 consensus [37], recommends administering 1500 units per angiosome, together with all supplementary recommendations.

Specific ocular treatment involves retrobulbar (intraconal), peribulbar (extraconal), and extraorbital HYAL injections. Retrobulbar (RB) HYAL is considered the first-line intervention [47], although its use remains controversial [37] due to the limited diffusion of HYAL into the

Table 5 Therapeutic options with corresponding class of recommendation (COR) and level of evidence (LOE) in the management of neuro-ophthalmic involvement

Therapeutic options	COR	LOE	References
Intraocular pressure reduction	1	B	[10, 39, 61, 71]
Anti-platelet therapy	1	BA (ischemic stroke)	[32, 39, 61, 71]
HYAL cutaneous retrobulbar/peribulbar supraorbital/ supratrochlear	1	B	[10, 39, 61, 71]
Ocular massage	1	C	[10, 39, 61, 71]
Vasodilators	2	C	[18]
Oxygen/hypercapnia therapy	1	C	
Selective intra-arterial thrombolytic therapy	2	B	[10, 39, 61]
Hyperbaric oxygen therapy (HBOT) in blindness	1	C	[18, 59–61]
Urgent contact with ophthalmologist or Hospital-based retina center with a stroke code team and interventional radiology.	1	C	[10, 38, 39, 61, 63, 71]
HBOT in stroke	1	C	[67]
-Acute phase of stroke not recommend.			
-Chronic phase, recommended in selected patients with documented areas of metabolic dysfunction	3	C	

optic nerve sheath [48]. Nevertheless, some authors regard this as a plausible theory, while others question the particular diffusion properties of RB HYAL [23]. RB administration typically involves preparing 1500 units [18, 33, 49] diluted in 2–5 mL of lidocaine, with a recommended dose of (900–1500 U/mL) per eye [18] injected into the inferolateral retrobulbar space using a cannula. Other studies have recommended a dose of approximately 800 units per eye [50, 51]. If RB injection is not feasible, at least a peribulbar (PB) or sub-tenons injection is recommended. However, there is no consensus regarding the optimal dose or route of administration.

Extraorbital (EO) HYAL injections directed to the supratrochlear (ST) and supraorbital (SO) arteries are currently regarded as the most effective recommendation based on existing evidence [18]. ST and SO injections can be administered at a dose of 500 units per area per hour [18, 33, 35], for a maximum of three administrations. Patients should be reassessed every 20 min, and if no clinical improvement is observed, repeat treatment may be performed at 60 min intervals. Capillary refill (approximately 2seconds) and prick testing should be used to assess reperfusion in the ST/SO territories. Treatment may be continued until reperfusion is achieved, with a maximum of 6–8 cycles. Based on the authors' protocol, the cutaneous area of origin should be treated with 1500 units per angiosome every 20 min [35]. If peribulbar or sub-Tenon injection is not feasible, retrobulbar injection may be considered, using 900–1500 units diluted in 3–4 mL (maximum volume 5 mL). Patients should be reassessed every 20 min, with repeat treatment if reperfusion is not achieved or at hourly intervals, up to a maximum of 6–8 cycles. RB-HYAL has relative contraindications, including HYAL allergy, anticoagulation, and lack of operator experience, and carries risks such as globe perforation, vascular or nerve injury, infection, and vasovagal reactions.

Ocular Massage (COR I; LOE C) Once the medications are administered, ocular massage should be initiated [38]. This technique helps reduce IOP and increases blood flow in the arterioles, potentially dislodging the embolus. However, current results across various case series of CRA occlusion remain mixed and lack robust evidence [52]. A case has been reported of vision recovery after HA-induced blindness following aggressive ocular massage [53].

We recommend the following simple digital massage technique for non-ophthalmologists [54], with consideration of a more aggressive approach in cases of complete vision loss. Firm pressure should be applied to the eyeball through the closed eyelids, sufficient to indent the globe by 2–3 mm. For a more aggressive massage, the pressure may indent the eye by up to 5 mm, combined with a one-second rotational movement per cycle. Firm pressure should be maintained for 5 to 15seconds, followed by rapid release. This cycle should be repeated for at least five minutes, assessing whether the patient's vision improves, and continued until recovery is achieved. Potential complications of intense ocular massage include retinal detachment, Valsalva retinopathy, and lens dislocation.

Vasodilators (COR II; LOE C) [18] Vasodilators may be used to facilitate embolus mobilization [52]. They are contraindicated in cutaneous involvement until the skin lesion has resolved [20], but in ocular cases they may be considered to displace the embolus as distally as possible. Care must be taken to avoid compromising choroidal perfusion pressure, defined as the difference between mean arterial pressure (MAP) and IOP. Among calcium channel blockers, benzothiazepines such as diltiazem are recommended, as they exert minimal effects on MAP. Phosphodiesterase inhibitors are not advised due to reported cases of retinal vascular occlusion associated with sildenafil [55].

Oxygen / Hypercapnia Therapy (COR I; LOE C) Oxygen therapy can be administered via VMK-Venturi mask or low-flow nasal cannula when O_2 saturation falls below 94%. In ocular filler complications, a maximum oxygen concentration of 35% is recommended, together with the induction of hypercapnia through rebreathing with a paper bag [10, 56], with the aim of increasing arterial PCO_2 as a cerebral and ocular vasodilatory strategy, although robust supporting evidence remains limited. Oxygen supplementation aims to enhance O_2 delivery, while hypercapnia contributes an additional vasodilatory effect.

Selective Intra-Arterial Thrombolytic Therapy (SIATT) (COR I; LOE B) This technique is safe and effective but can only be performed in high-level hospitals with interventional radiology and in carefully selected patients (visual dysfunction grades B/C), as it is not free of complications. SIATT achieves re-permeabilization of the occluded artery in 100% of cases [41]. However, it only improves visual acuity in patients with residual vision at presentation. Approximately 42% of patients demonstrate improvement in visual acuity despite exceeding the recommended therapeutic window for optimal treatment (similar to stroke), whether treated with HYAL alone or in combination with urokinase [57, 58].

In contrast, patients presenting with complete loss of vision and no light perception, which typically reflects the absence of effective collateral circulation, have a markedly poorer prognosis and a low likelihood of meaningful visual recovery, making aggressive intervention more likely to be futile. Nevertheless, as long as some degree of visual function is preserved, all reasonable therapeutic options to promote reperfusion and potential recovery should be actively pursued, taking into account the associated risks and the technical feasibility of the intervention.

In a small case series [58] of supraselective HYAL administration into the ophthalmic artery, the authors concluded that even when patients are admitted early, it is extremely difficult to perform such a complex technique rapidly, as it requires prior imaging studies. Consequently, the 15–240 min ischemic window of the retina is usually surpassed. While proximal branches can be recanalized by catheter delivery, distal branches may remain occluded as they do not come into direct contact with HYAL. Patients without light perception failed to show any improvement, suggesting that the presence of collateral circulation or partial occlusions may improve prognosis despite prolonged ischemia and otherwise unfavorable factors.

This technique is not without risks, and the likelihood of procedure-induced thrombosis is significant. Ocular and eyelid motility improved in all patients, structures that can tolerate longer ischemic times.

In eight cases of cerebral infarction treated with SIATT for blindness [58], there was only one case of intracerebral hemorrhage following established infarction, possibly related to secondary vascular necrosis, increased intracranial pressure from thrombolytic injection, or the use of concomitant anticoagulation. Secondary cerebral emboli may also occur due to embolus fragmentation, underscoring the need for close follow-up.

If IATT is performed, the recommended dosage of HYAL ranges from 700 to 1500 units and/or urokinase 100,000 to 250,000 IU [58], combined with papaverine 30 mg.

Hyperbaric Oxygen Therapy (HBOT) (COR I; LOE C; as an adjunctive treatment) Combined treatment with HBOT in cases of filler-induced blindness has been associated with some degree of improvement in 41.4% of patients [2].

The optimal timing for initiating HBOT in CRA occlusion remains under debate, but it is generally recommended as an adjuvant therapy as early as possible, ideally within the first 24hours. The initial session should be performed at 2 ATA for 90 min with 5 min air breaks every 20 min in multiplace chambers, or 60 continuous minutes in monoplace chambers [59].

If no improvement in visual dysfunction is observed within 30 min, the pressure should be increased to 2.4 ATA while maintaining the treatment schedule. If there is still no improvement, pressure may be further increased to 2.8 ATA, and a U.S. Navy Treatment Table 6 may be attempted as a last resort. If no response is achieved, treatment can either be discontinued or continued depending on clinical judgment [59, 60]. If the patient shows improvement or the treatment is continued, reevaluation should take place after 4–6 days, and therapy should be suspended once stabilization of visual recovery has been reached [59, 60].

Others Anticoagulation with low-molecular-weight heparins (LMWH) has been recommended by some authors

[61], and should always be considered after APT in cases where the occlusion persists. Alprostadil, a prostaglandin used as a vasodilator and antiplatelet agent in deep inferior epigastric perforator procedures, currently lacks strong evidence but has been reported in isolated cases to yield favorable outcomes in ophthalmic artery occlusion [62].

Contact High-Level Hospital Grade III-IV Hospital-based retina center with a stroke code team and interventional radiology (COR I; LOE C) [10, 38, 39, 61, 63]

Contact an ophthalmologist or a hospital-based retina center [38] as early as possible, as this is the first step in some protocols [10, 38, 39]. The patient with a hospital transfer card (Fig. 5) should be referred to a hospital with a specialized ophthalmology service or a dedicated retina unit equipped to provide immediate diagnostic testing as well as intraocular or interventional treatments, including retrobulbar injections or anterior chamber paracentesis. Referral should also involve the Neurology service or the Stroke Code team, since retinal artery occlusion is considered a form of retinal stroke [63]. In addition, access to Interventional Radiology or Neuroradiology is important for potential intra-arterial therapies, advanced interventions, and vascular imaging of the brain and orbital vessels [63].

Neurological Treatment

Stroke There is currently no consensus regarding the optimal treatment of stroke caused by HA. However, by drawing parallels to other ischemic embolic events that share similar pathophysiological mechanisms with ischemic stroke [24], a series of adapted management strategies can be proposed. Most of these measures are derived from established ischemic stroke clinical guidelines, while evidence specific to HA-related embolic stroke is limited and primarily restricted to studies on supraselective endovascular therapy, which provide the main HA-specific rationale for thrombolysis through the addition of HYAL. In addition, the high reported association between blindness and subclinical or overt stroke further supports the need for systematic neurological evaluation and tailored management in this patient population.

HOSPITAL TRANSFER CARD

Patient Name : _____
Age : _____ Sex : _____
Date / Time : _____
Filler (type) : _____
Volume (ml) : _____
Skin involved : [ ] YES [ ] NO

BLINDNESS : [ ] YES [ ] NO
Classification: _____

STROKE : [ ] YES [ ] NO
Classification: _____

TREATMENT ADMINISTERED

Hyaluronidase (dose & location): _____
Time Hyaluronidase Administered : _____
Antiplatelet Agents (drug & dose): _____
Eye Drops (type & dose) : _____
Vasodilators (drug & dose) : _____
Ocular Massage (Yes/No + time) : _____

Fig. 5 Hospital transfer card for emergency referral in neuro-ophthalmic ischemic complications

General measures [32] include maintaining oxygen saturation (Sat O2) above 94% with supplemental oxygen if necessary. Hypotension should be avoided through the use of crystalloids, while hypertension should be treated if systolic blood pressure exceeds 185 mmHg or diastolic blood pressure exceeds 110 mmHg. Hyperthermia above 38°C should be addressed with antipyretics, and hypoglycemia (<60 mg/dl) should be corrected, as it worsens prognosis. Similarly, hyperglycemia should be maintained below 140–180 mg/dl. In the present review, the authors focus on therapeutic considerations that are specific to HA-related embolic stroke, particularly supraselective thrombolysis with HYAL. Intravenous thrombolysis (IVT) may be considered in selected patients [32] and carries a Class of Recommendation I in current AHA stroke guidelines; however, in the context of HA-related embolic stroke, the supporting evidence remains limited (LOE C). Standard stroke management measures are therefore not detailed individually, as they are well established and comprehensively addressed in existing stroke management protocols.

The safety and efficacy of thrombolysis are well-established within the first 3 hours following a stroke, with the window extended up to 4.5hours for selected patients. The age range for thrombolysis is between 18 and 80 years. In cases of severe stroke, thrombolysis is indicated, and in moderate disabling strokes, thrombolysis may be considered if it provides clinical benefit, once hemorrhagic risk has been excluded. Thrombolysis is not contraindicated in patients on monotherapy or dual APT (AAS and clopidogrel), although the risk of cerebral hemorrhage is increased.

A cerebral CT scan is essential for excluding hemorrhagic processes and the presence of established lesions with severe hypoattenuation or hypodensity, which would indicate irreversible damage and futility of thrombolytic treatment [32]. IVT is contraindicated beyond 4.5hours, in patients with previous traumatic brain injury, suspected space-occupying lesions, personal history of cerebral hemorrhage, anticoagulant therapy, coagulopathies, active hemorrhage, major surgery in the last two weeks, or during pregnancy [32].

Intra-arterial thrombolysis is beneficial for selected patients up to 6hours after the event. However, the intra-arterial dose is not well defined and may be an option when

intravenous fibrinolysis is contraindicated, though outcomes remain uncertain.

Initial APT with 325 mg of AAS is recommended within the first 24–48hours, delayed to 24hours if the patient has received thrombolysis; however, early administration does not contraindicate thrombolysis.

Anticoagulation is not recommended [32], nor are neuroprotective agents, HBOT, vasodilators, or pentoxifylline. Antithrombotic prophylaxis with LMWH is recommended for immobilized patients.

Analyzing ischemic stroke guidelines and applying them to HA-induced embolic strokes, it can be stated that in addition to conservative ischemic stroke management and excluding IVT, SIATT with HYAL combined with urokinase (dosages not well established for stroke and even less so for HA-induced stroke) within the first 6hours may represent the most appropriate approach [64] (COR II; LOE B) [10, 39, 61]. Furthermore, HYAL may also be useful in HA-induced vasospasm, as it has implications for removing the endothelial glycocalyx [65, 66].

Mandatory APT in vascular occlusion is not a contraindication to this technique, except in cases of extreme age, specific high hemorrhagic risk, CT findings of established ischemic infarction, or hemorrhagic transformation. These considerations may justify withholding the therapy. This intervention is only feasible in high-technology centers, many of which lack experience. Conventional intravenous thrombolysis is not entirely excluded, since HA carries a significant prothrombotic component, but it should be considered off-label and only within ischemic stroke thrombolysis guidelines, with risks clearly assumed in patients with severe clinical compromise.

In the absence of interventional radiology capable of performing SIATT, when the event-to-catheterization time exceeds 6hours (time-dependent pathology), or in patients with low NIHSS scores (0–5), in whom no clear benefit is expected, or very high NIHSS scores (21–25), in whom the risk of hemorrhagic transformation is substantial, SIATT is not recommended. In these scenarios, conservative management is the preferred treatment option [36].

Adjunctive HBOT is not recommended in the acute phase of stroke (COR I; LOE C). In the chronic phase, in selected patients with documented areas of metabolic dysfunction, HBOT may be considered under clinical trial settings (COR III; LOE C) [67]. Current evidence is insufficient to confirm that HBOT alters outcomes in acute ischemic stroke [68]. A recent meta-analysis confirmed the lack of robust evidence but did not entirely rule out potential clinical benefits [22].

If blindness coexists with stroke, adjunctive HBOT may be considered for the visual complication, as it does not cause neurological harm and does not increase adverse event rates compared with controls [22]. However, authors recommend standard FIVO hyperbaric oxygen (FiO_2) at 2 ATA as the primary approach.

Cerebral Venous Thrombosis Venous infiltration by HA induces inflammatory thrombophlebitis [69]. Through venous migration, the HA embolus can reach the cerebral venous circulation, potentially leading to venous sinus thrombosis. This condition presents with cerebral edema, signs of intracranial hypertension, and focal neurological deficits [70]. The appropriate treatment consists of therapeutic-dose anticoagulation with LMWH [69, 70], along with management of intracranial hypertension.

Discussion

Ophthalmic vascular occlusion (OVO) secondary to HA filler injection is a devastating complication that requires immediate recognition and intervention. The present review highlights the central importance of early diagnosis, temporal classification of ischemia, and tailored management strategies. Embolic events may occur immediately through direct intra-arterial injection or later due to embolus fragmentation after HYAL administration or migration through arteriovenous shunts, including patent foramen ovale or pulmonary arteriovenous malformations [3, 5, 6]. This pathophysiological variability underscores the need for vigilance not only in the acute setting but also during the subacute period in patients presenting with unexplained neuro-ophthalmic symptoms.

Clinical outcomes depend on the number of vessels involved, the vascular territory affected, and the volume of HA injected. Total blindness (no light perception) most commonly reflects involvement of the OA or the CRA and is associated with a poor prognosis. In contrast, partial visual loss typically indicates occlusion of branches of the CRA, and blurred vision is more often associated with involvement of the PCA; both patterns are generally associated with a more favorable prognosis due to the potential for collateral circulation. Accordingly, the degree and pattern of ocular involvement represent critical prognostic factors [11, 18]. When blood flow to the muscular branches is compromised, ophthalmoplegia and strabismus may occur. Similarly, occlusion of branches supplying the eyelid and periocular tissues may result in eyelid dysfunction and periocular symptoms; these non-retinal tissues generally tolerate ischemia better and are therefore associated with a more favorable functional recovery compared with retinal ischemia [11, 18].

Overall, poor outcomes are most strongly predicted by complete vision loss at presentation, involvement of the OA or CRA, absence of collateral circulation, larger embolic burden, and delayed initiation of treatment.

Consistent with this, only approximately 17% of untreated CRAO patients experience any degree of visual recovery [18].

In a review by Doyon et al. [2] including 365 cases of vision loss, visual outcomes were reported in 318 patients. Complete visual recovery was observed in 6.0% of cases, partial improvement in visual acuity in 25.8%, and no visual recovery in 68.2% of patients. In the study by Rahman et al. [26] (FAASS), a predictive model for visual outcomes was developed. In this analysis, HYAL dose and time to treatment demonstrated limited predictive value, whereas patient age and injection site were the strongest predictors of visual recovery.

The temporal classification of blindness provides valuable prognostic insight. Fulminant events, occurring within the first 10 min, are the most common and reflect direct canalization, while delayed or late cases are associated with progressive embolus migration [7, 8]. Prognosis is strongly related to the degree of residual vision and collateral circulation [11, 18]. Although ophthalmoplegia recovers in up to 77% of cases [12], CRAO remains associated with irreversible blindness in most patients. The ischemic tolerance of the retina, estimated between 15 and 240 min [14–17], emphasizes the extreme time sensitivity of therapeutic intervention.

Neurological involvement, present in approximately 24% of cases [22], expands the clinical impact of these events beyond ophthalmology. The frequent involvement of the middle cerebral artery [3] and the under-recognized presence of subtle neurocognitive changes highlight the importance of systematic neurological evaluation and imaging in all cases of visual loss. Classifications such as FAASS [26] and the proposed Fakih-Madero Neuro-Ophthalmic Evaluation (Fig. 4), which integrate ophthalmic, neurological, and functional parameters, may facilitate more consistent patient stratification and improve clinical decision-making.

Despite the existence of multiple proposed treatment algorithms, no standardized or universally effective therapy has been established for filler-induced blindness [33, 34]. Current management is largely extrapolated from ischemic stroke and retinal artery occlusion protocols [32]. Initial ophthalmic measures include IOPR, ocular massage, oxygen therapy, vasodilators, APT, and HYAL injection at multiple levels, including extraorbital (ST and SO), extraconal-PB, and intraconal-RB sites [18, 37, 47]. Time remains the critical determinant of success, with HYAL administration being the only intervention consistently associated with improved outcomes [13]. Early administration of HYAL is likely the single most important factor associated with favorable visual outcomes. Therefore, treatment should not be delayed and must be initiated immediately after the event, ideally in the same chair where the complication occurred.

The management of filler-induced ophthalmic vascular occlusion by any by trained aesthetic medicine practitioners should follow the general treatment measures described previously and HYAL injection in extraorbital (ST and SO) and extraconal (PB) sites. These measures are relatively safe, technically feasible, and can be initiated immediately at the point of care, which is critical given the extremely narrow therapeutic window. However, the question arises whether aesthetic physicians should also be trained and authorized to perform intraconal (RB) injections. On one hand, RB administration of HYAL may provide a more direct and potentially more effective route to dissolve embolic material within the ophthalmic artery (OA) or its branches. This technique could theoretically improve outcomes in cases of CRAO, particularly when initiated without delay. On the other hand, RB injections carry significant risks, including globe perforation, retrobulbar hemorrhage, optic nerve damage, and inadvertent spread of embolic material, which may result in permanent visual or neurological injury. Such risks are typically managed within the scope of ophthalmologists, oculoplastic surgeons, and other physicians with formal training in orbital and periorbital anatomy.

For this reason, many authors recommend a tiered approach: aesthetic medicine doctors should perform all immediately accessible measures, including HYAL at the ST, SO, and PB levels, while intraconal-RB injections should be reserved for ophthalmologists or physicians with specialized orbital training. This approach maximizes the chances of early intervention without exposing patients to the potentially catastrophic complications of a technically demanding procedure performed by inadequately trained practitioners.

Nevertheless, the debate remains unresolved. Some experts advocate for broader RB training among aesthetic physicians, arguing that the time required to refer a patient to an ophthalmologist may exceed the ischemic tolerance of the retina, which is estimated at 15 to 240 min [18]. Others caution that the risks outweigh the potential benefits when performed outside a specialist setting. Ultimately, whether all aesthetic physicians should be trained in retrobulbar techniques is a question that demands further multicenter study, standardized training protocols, and consensus guidelines. Until then, the prevailing recommendation is that aesthetic physicians initiate all non-retrobulbar measures immediately and refer patients for RB injection to ophthalmologists or other appropriately trained specialists.

Advanced strategies, such as IATT with HYAL, with or without urokinase, have shown potential for achieving

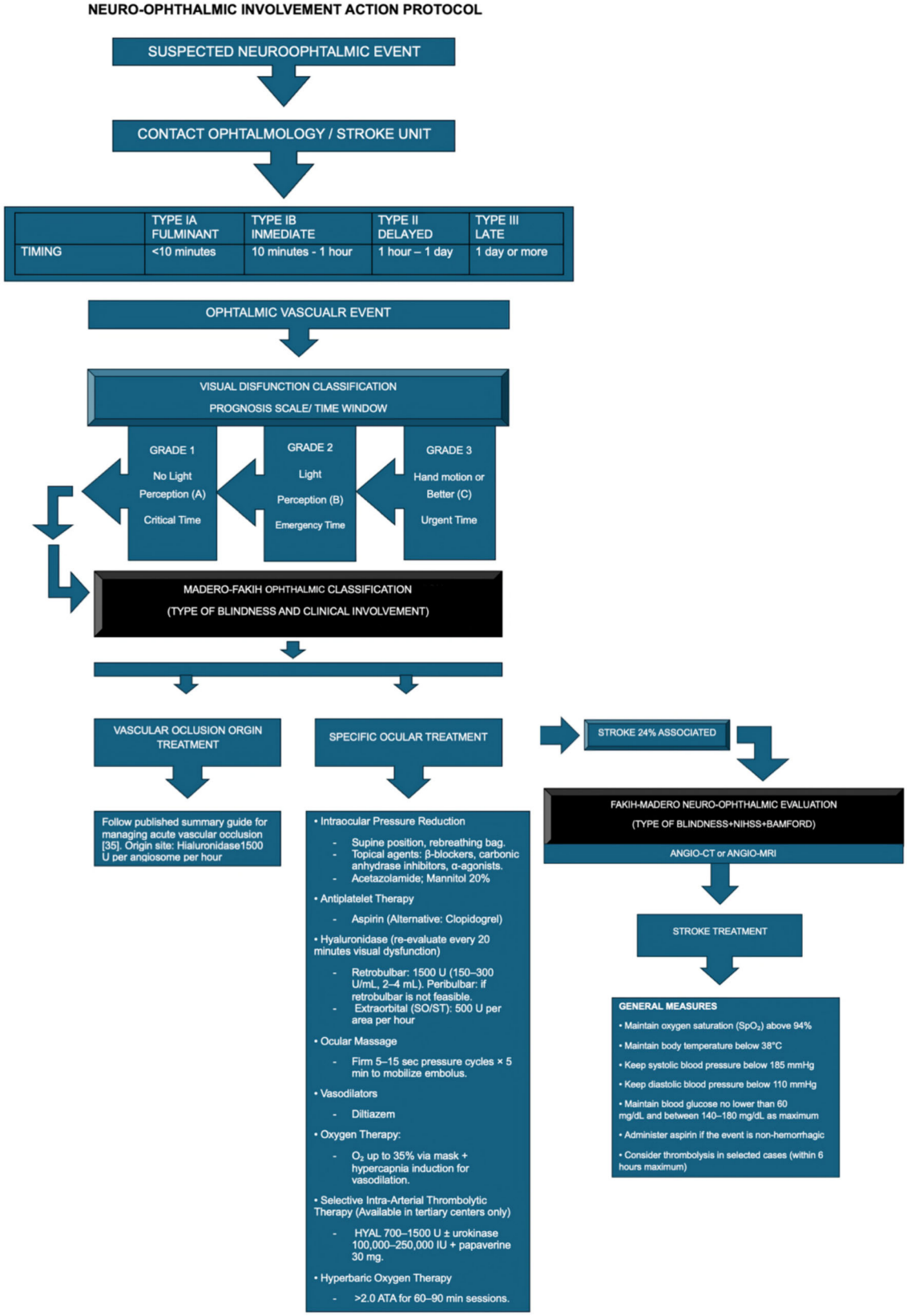

Fig. 6 Summary guide for the management of filler-induced neuro-ophthalmic involvement. *MRI* Magnetic resonance imaging; *VAS* Visual analogue scale; *LOAE* Late onset adverse event; *Hrs* Hours

recanalization, but these techniques are technically demanding and often exceed the therapeutic ischemic window [58]. Adjunctive HBOT may improve outcomes in approximately 41% of patients [2], although supporting evidence remains limited.

In cases with neurological involvement, stroke protocols should be applied, with thrombolysis considered only in selected patients [26, 32]. Intra-arterial thrombolysis and thrombectomy may be appropriate in specialized centers, though evidence for HA-specific strokes remains scarce [64–66]. Cerebral venous sinus thrombosis, although rare, requires anticoagulation with low-molecular-weight heparin [69, 70]. A summary guide for the management of filler-related neuro-ophthalmic involvement is presented in Fig. 6. A summary of therapeutic options with corresponding class of recommendation (COR) and level of evidence (LOE) in the management of neuro-ophthalmic complications is presented in Table 5.

The proposed classification systems aim to standardize the reporting and characterization of neuro-ophthalmic complications related to dermal filler embolization, in order to facilitate more robust future analyses and enable clearer conclusions regarding treatment efficacy in relation to timing and clinical severity. At present, the available literature is highly heterogeneous, with inconsistent definitions, variable outcome measures, and non-uniform classification of events. This lack of standardization has limited the ability of current studies and meta-analyses to draw definitive conclusions regarding optimal management strategies and prognostic factors.

Moreover, these complications are rare but severe, making it extremely difficult to generate patient series with sufficient statistical power for formal validation. Meaningful validation would likely require large, multicenter registries and coordinated international data collection efforts. As a result, many of the recommendations and classifications proposed in this review are necessarily based on expert opinion derived from the best available evidence in the current literature. Only through harmonized data collection and interdisciplinary collaboration will it be possible to establish evidence-based standards for this challenging condition. Thus, the classification of severity, localization, and neurological involvement will ultimately determine prognosis and allow a more precise assessment of the risk–benefit balance of such treatments. These classifications should therefore be viewed as a pragmatic framework to support clinical decision-making and future research, rather than as definitively validated prognostic or therapeutic models.

Conclusion

In OVO caused by fillers, blindness is a medical emergency that requires immediate treatment at the site of origin. Initial management should include IOPR, APT, ocular massage, vasodilators, and the injection of HYAL into the SO, ST, and RB regions. The patient must then be transferred without delay to a high-level hospital (Grade III–IV) for further treatment and comprehensive ophthalmic evaluation, as well as to rule out neurological involvement through clinical examination and imaging studies. The management of HA-induced stroke remains poorly defined, and the risk–benefit ratio of any proposed therapies must be carefully considered. Given the increasing incidence of this complication due to the widespread use of fillers, the clinical classification of neuro-ophthalmic involvement is crucial for better patient stratification, which will ultimately support more consistent and evidence-based conclusions in the future.

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Declarations

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Ethics Approval This article does not contain any studies with humans or animals performed by any of the authors.

Consent for Publication All photographs do not require any consent for the publication.

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