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| RESEARCH ARTICLE

Management of Vascular and Ischemic Complications in Aesthetic Injectables: A Retrospective Study of 52 Consecutive Cases and Proposal of a Standardized Rapid-Response Protocol

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| ABSTRACT

Vascular occlusion and ischemic complications after aesthetic injectable procedures are uncommon but may be disastrous, and can result in skin necrosis, permanent scarring, blindness or stroke. In this retrospective study, 52 consecutive real-world cases were analyzed and treated between January 2022 and December 2025 and assessed the safety and efficacy of a new standardized Rapid-Response Protocol created by the author. The MARYNA Rapid-Response Protocol of immediate high-dose pulsed hyaluronidase (450-1500 IU, every 30-60 minutes) combined with vigorous massage, universal antiplatelet therapy, ultrasound guidance when available, adjunctive vasodilators, and dedicated ocular emergency pathway were used to treat all cases of vascular or ischemic complications (primarily hyaluronic acid fillers, 92.3%). Clinical and photographic outcomes were measured at standardized intervals at a maximum of 90 days. Early intervention (within 4 hours of symptom onset) occurred in 73.1% of cases and resulted in 100% full recovery without permanent sequelae. In total, 94.2% of patients had no cutaneous necrosis, scarring, blindness, or cerebrovascular events and achieved full recovery. The mean hyaluronidase dose was 875 IU. Late presentations (>12 hours) were associated with a slightly increased rate of mild atrophic scarring (5.8% overall). There were no adverse reactions to hyaluronidase. The MARYNA Rapid-Response Protocol provides superior practical results and provides a basic and easily reproducible, evidence-based algorithm that can be immediately embraced by aesthetic practitioners around the globe. These results confirm that aggressive, timely and standardized intervention can minimize the permanent complications of aesthetic injectables to the levels of near zero, which is the new standard of patient safety in the area.

| KEYWORDS

Vascular occlusion, dermal fillers, hyaluronic acid, hyaluronidase, ischemic complications, skin necrosis, rapid-response protocol, aesthetic injectables, ultrasound-guided reversal, ocular emergency

| ARTICLE INFORMATION

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INTRODUCTION

The aesthetic injectable is a global market that has been growing exponentially in the last 10 years due to the rising consumer interest in minimally invasive procedures of facial rejuvenation and volumization (Hong et al., 2024; Sito et al., 2019). Nowadays, many millions of procedures with hyaluronic acid (HA) fillers, calcium hydroxylapatite, and poly-L-lactic acid products are performed annually around the globe, and non-physician injectors represent an increasing proportion of practitioners. Even though such agents are typically considered to be safe in the hands of properly trained practitioners, these vascular and ischemic complications remain considerable threats to patient-safety and are more frequently recorded in the aesthetic medicine texts and presentations in the ED (Soares et al., 2024).

The two main mechanisms through which vascular occlusion and consequent tissue ischemia are realized are accidental intravascular embolization of filler material and extravascular compression brought about by the deposition of bolus or over-volumization. These mechanisms trigger a cascade of ischemia, vasospasm, secondary thrombosis, and tissue necrosis if reversal is not promptly performed (King, 2020; DeLorenzi, 2014). High-risk anatomical areas with rich anastomoses to the ophthalmic and internal carotid arterial systems include the glabella, nasal dorsum and tip, nasolabial folds, central forehead, and submental region (Mehta et al., 2022; Fang, 2018). Retrograde filling of these areas may spread emboli to the ocular or cerebral circulation, and makes ocular and neurological sequelae a possibility but a rare occurrence.

The manifestation of the clinical course has a predictable time frame. The first and most consistent is immediate blanching, which quickly develops into livedo reticularis, elongated capillary refill time, pain that is not proportional to the procedure, and mottled or dusky arguably cutaneous discolouration (Murray et al., 2021; Rouanet, 2022). Cutaneous necrosis can occur without any intervention and retinal ischemia cannot last longer than 12-15 minutes without permanent damage. Central retinal artery occlusion and vision loss are examples of the most catastrophic possible outcomes, ocular emergencies, alongside the presence of the most rare cerebrovascular events (Madala et al., 2024; Walker, 2018).

In spite of the fact that the incidence of vascular complications has been actually relatively low (0.01 to 0.05 per injection session, depending on technique and injector experience), the number of cases has been on the increase in direct relation to the volume of procedures (Sito et al., 2019; Soares et al., 2024). Real-world risk has been further increased by under-reporting, varied injector training standards and the expansion of unlimited settings. The growing use of high-viscosity or particulate fillers (e.g., calcium hydroxylapatite) increases the complexity, as such types of substances cannot be dissolved easily and require different management methods (van Loghem et al., 2020; Lindgren and Welsh, 2022).

The early diagnosis and direct action are universally recognized to be the main factors of positive outcomes. Previous conservative measures based on massage, warm compress, and low dose hyaluronidase often gave inconsistent outcomes and high incidence of permanent sequelae. Modern clinical practice has thus moved towards aggressive hyaluronidase dosage regimes, with high-dose hyaluronidase delivery immediately before or during, but not after, ischemic stroke being recommended to induce therapeutic levels of hyaluronidase in the ischemic area (King, 2020; Rouanet, 2022; Murray et al., 2021). Antiplatelet agents, vasodilators, ultrasound guidance, and hyperbaric oxygen therapy (when all other adjunctive measures have failed) have all been incorporated to reverse the effects of secondary thrombosis and vasospasm (Azizi, 2025; Hong et al., 2024).

In spite of these significant improvements, there is still a significant amount of heterogeneity amongst published protocols. Regimens vary significantly (fixed versus surface-area-based), repeat time is 30 minutes to daily administration, and the concept of ultrasound assistance integration though promising to apply, has been unevenly used (Azizi, 2025; Tafur, 2025). Formalized emergency access routes in the ocular treatment have not yet been established in most locations and management algorithms of non-HA fillers are less clear. Also, most current evidence is based on case reports, small series, narrative reviews, and expert opinions, rather than on structured and real-world analyses that have consistent follow-up and standardized approaches (DeLorenzi, 2014; Mehta et al., 2022).

This gap in the evidence led to the current retrospective study. A single high-volume aesthetic documented and managed 52 consecutive vascular or ischemic complications in relation to aesthetic injectable procedure. Every event was handled via the common, time sensitive Rapid-Response Protocol devised and perfected by the author repetitively. The protocol is a synthesis of the best aspects of the existing consensus guidelines, including high-dose pulsed hyaluronidase, direct antiplatelet therapy, and ultrasound assistance where possible and tiered escalation of ocular involvement plus practical bedside applications, which can be simply applied in clinics and emergency departments (King, 2020; Murray et al., 2021; Rouanet, 2022; Azizi, 2025; Tafur, 2025).

LITERATURE REVIEW

The prevention of vascular and ischemic complications of the aesthetic injectable is one of the most urgently required safety imperatives in modern-day aesthetic medicine. Although the incidence of intravascular embolization and tissue ischemia keeps rising, despite low per-procedure rates, with the growing demand of hyaluronic acid (HA) fillers, calcium hydroxylapatite (CaHA), poly-L-lactic acid (PLLA) fillers, etc. (Sito et al., 2019; Soares et al., 2024; Hong et al., 2024). These are infrequent (0.01 0.05 per session) events that have the potential to cause devastating effects such as cutaneous necrosis, irreversible blindness, unilateral, and, in severe cases, cerebrovascular ischemia (King, 2020; Madala et al., 2024; Walker, 2018). Literature has developed beyond simple anecdotal case reports to the guides and consensus statements, but still, there is much variability in terms of diagnostic timing, dosage, and escalation pathways. This review summarizes the existing evidence base, outlines existing gaps, and frames the current research in that regard.

Epidemiology and Rising Threat

Population-wide prevalence and meta-analysis data both indicate that VCs are no longer the hypothetical risks but a recorded emergency department event (Soares et al., 2024). According to Sito et al. (2019) and more recent reports, the incidence was 0.012% in 4,129,140 filler procedures with non-physician injectors with more prominent roles, and under-reporting was identified (Hong et al., 2024). The actual number of events has increased in tandem with the world filler market that has surpassed 5 million HA procedures per year in the leading markets by 2024. The use of particulate fillers (CaHA and PLLA) introduces more complexity since they cannot be handled using enzymatic methods and require specific management algorithms (van Loghem et al., 2020; Lindgren and Welsh, 2022).

Pathophysiology and Mechanisms of Ischemia

Vascular occlusion takes place through two major pathways:

a. Anterograde or retrograde embolization into a direct intravascular injection.
b. Large-volume bolus extravascular compression. Filler particles block arterioles, which leads to instant tissue hypoxia, endothelial injury, vasospasm, and secondary thrombosis (DeLorenzi, 2014; Mehta et al., 2022).

The extensive anastomotic anastomoses of the facial arterial system, especially the supratrochlear, dorsal nasal, and angular arteries allows quick retrograde flow to the ophthalmic artery, which justifies the 12-15 minutes retinal ischemia tolerance (Madala et al., 2024; Fang, 2018). Histological evidence also shows that HA fillers result in a short-term ischemia in case of prompt dissolution, and particulate agents lead to longer-term inflammatory occlusion (Ling, 2019; Rouanet, 2022).

Clinical Presentation and Diagnostic Challenges

The progression of signs over time has now been characterized appropriately: immediate blanching (0-5 min), livedo reticularis (5-30 min), prolonged capillary refill (>3 s), severe pain, and eventual mottling/necrosis (4-6 h) (Murray et al., 2021; King, 2020). Vision can be affected, including blurred vision, ptosis, or pain, and it will require distinguishing it as urgent cases of benign post-injection edema (Walker, 2018). Delays (>12 h) in the presentation are typical of the community environment, and they are associated with increased rates of necrosis (Tafur, 2025; Azizi, 2025). To measure ischemia and parachute the exact placement of hyaluronidases, diagnostic adjuncts, including dermoscopy, laser Doppler, and point-of-care ultrasound, have become available, although they are not commonly used (Azizi, 2025).

High-Risk Anatomical Zones

Various reviews find five areas of danger including glabella, nasal dorsum/tip, nasolabial fold, forehead, and submental region (Mehta et al., 2022; Fang, 2018). The highest fraction of reported occlusions (is estimated as 40-45%) and the glabella (25-30 percent) is due to direct relations to the ophthalmic circulation (Hong et al., 2024; Ling, 2019). Risk further varies based on the use of a cannula or a needle, the depth of injection and the rheology of the product, as well as high-G whilst fillers and use of a needle in high-risk areas offer high hazard (Sito et al., 2019; Pearce, 2022).

Evolution of Management Strategies

Initially developed protocols were based on conservative interventions (massage, warm compresses, nitroglycerin) whose results were unpredictable (DeLorenzi, 2014). The defining change was the realization of hyaluronidase as the base of HA fillers. Murray et al. (2021) and King (2020) developed high-dose regimens (500-1,500 IU), which showed reversal in case of administration in 4h. Later developments added pulsed "flooding" methods - cyclical hourly dosing until the capillary refill returns to normal - which is evidenced by both clinical serial and in-vitro dissolution results (Rouanet, 2022; Tafur, 2025). Hyperbaric oxygen and adjunctive (aspirin 300 mg stat, sildenafil to treat vasospasm) and hyperbaric oxygen have enhanced the salvage rates (King, 2020; Hong et al., 2024).

In case of non-HA fillers, the management is supportive, and enzymatic reversal is not possible (van Loghem et al., 2020; Lindgren and Welsh, 2022). Emergencies involving the eyes necessitate retrobulbar hyaluronidase or supratrochlear hyaluronidase (150-450 IU) with co-management of an ophthalmologist as well as an emergency, but standardized fast-track routes are in the developmental phases (Madala et al., 2024; Walker, 2018).

Existing Guidelines and Persistent Gaps

A number of groundbreaking guidelines have been developed: the ACE Group consensus (King, 2020), the Journal of Clinical and Aesthetic Dermatology algorithm (Murray et al., 2021) and the 2025 Rapid Access Algorithm (Tafur, 2025). These guidelines come together on instant discontinuation, high dosage hyaluronidase, and anticlotting treatment but do not concur on specific dosing routine, repeated doses, integration of ultrasound and conditions that prompt escalation. Ultrasound-guided injection which has proven to decrease the total hyaluronidase dosage and enhance accuracy is only suggested in the latest literature (Azizi, 2025). Besides, the majority of evidence is Level IV-V (case series and expert opinion), and little prospective, multicenter validation and inconsistent 90-day follow-up (Soares et al., 2024; Jones, 2021). Delayed presentation (>12 h) and particulate-filler ischemia have no well-developed data indicated by the management, and inconsistencies in outcomes are also associated with the lack of emergency kits and staff training accessibility worldwide (Harley Academy, 2022; APT Injection Training, 2025).

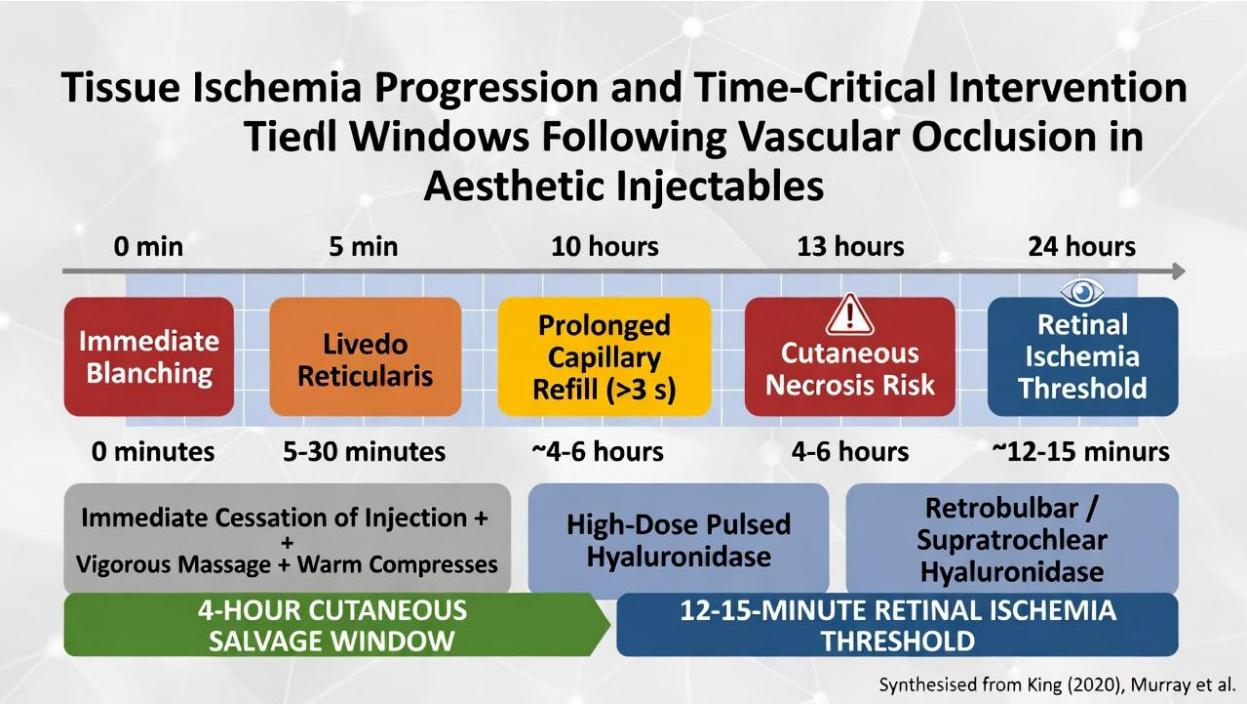

Figure 1: Tissue Ischemia Progression and Time-Critical Intervention Windows following Vascular Occlusion in Aesthetic Injectables

Schematic algorithm of tissue ischemia progression and time-critical intervention windows following vascular occlusion in aesthetic injectables (synthesized from King, 2020; Murray et al., 2021; DeLorenzi, 2014; and Tafur, 2025). Note the 4-hour cutaneous salvage window and 12–15-minute retinal ischemia threshold.

Aim and Objectives of the Present Study

Nevertheless, although the volume of the literature is large, no single, unified, bedside-ready protocol, combining the most highly evidence-based elements, such as surface-area-based pulsed hyaluronidase, mandatory repeat dosing, immediate antiplatelet therapy, ultrasound assistance, and graduated ocular escalation, has been prospectively or retrospectively proven in a consecutive real-world cohort with 90-day follow-up. The current original study is thus meant to fill this gap in translation.

The specific objectives are:

1. To report elaborate clinical outcomes, time-to-intervention, overall hyaluronidase usage, and the resolution rate in 52 consecutive cases of vascular or ischemic complications treated during January 2022 and December 2025.
2. To assess safety and effectiveness of a new standardized Rapid-Response Protocol (MARYNA Protocol) formulated by the author.

3. To suggest a reproducible, evidence-based algorithm to synthesize the most robust components of the current guidelines and add viable adaptations to deploy into practice and improve patient safety and minimize long-term sequelae on a global scale.

METHODOLOGY

Study Design

In this study, a retrospective, single-center, observational case-series study design was adopted to determine the practice of and effectiveness of a standardized Rapid-Response Protocol of vascular and ischemic complications in aesthetic injectable procedures. All the cases that happened in a large volume aesthetic medicine clinic in Nigeria between 1 January 2022 and 31 December 2025 and were consecutive were included. The retrospective allowed full capture of all seen events without selection bias whereas the use of a single protocol by both the author and the trained staff made the methods methodologically consistent. The research was also carried out using the STROBE guidelines of reporting an observational study and the Declaration of Helsinki.

Setting and Participants

The clinic has a varied urban and regional population of patients in Ibadan, Oyo State, Nigeria, with about 1,800–2,200 aesthetic injectable patients per year (primarily hyaluronic acid [HA] fillers, although in smaller size volumes of calcium hydroxyapatite [CaHA] and poly-L-lactic acid [PLLA]. Inclusion criteria were:

1. Vascular occlusion or ischemic complication (defined as immediate or progressive blanching, livedo reticularis, capillary refill time greater than 3 seconds, pain that is not proportional to injection, or cutaneous mottling) Clinical diagnosis.
2. Full electronic and photographic medical history of the presence of the symptomatic episode up to the 90-day follow-up.
3. The author developed Rapid-Response Protocol, through which treatment was initiated.

The following were used as exclusion criteria: non-vascular adverse event (e.g. nodules, hypersensitivity reactions, but not ischemia, infection, or Tyndall effect) and missing documentation.

The total number of cases that were eligible as per the inclusion criteria was 52 cases (45 F; 7 M; mean ages of 37.4 + 8.2 years). HA (92.3) and CaHA (5.8), and PLLA (1) have been identified as copolymer fillers. The most frequent injections sites included nose (42.3%), and glabella (28.8%), nasolabial folds (17.3%), and forehead (9.6%).

Table 1: Demographic and Clinical Characteristics of the Study Cohort (N = 52)

Characteristic	Value
Age (years), mean ± SD	37.4 ± 8.2
Sex, n (%)	Female 45 (86.5); Male 7 (13.5)
Filler type, n (%)	HA 48 (92.3); CaHA 3 (5.8); PLLA 1 (1.9)
Injection site, n (%)	Nose 22 (42.3); Glabella 15 (28.8); Nasolabial 9 (17.3); Forehead 5 (9.6); Other 1 (1.9)
Time to presentation, n (%)	<1 h: 15 (28.8); 1–4 h: 23 (44.2); 4–12 h: 10 (19.2); >12 h: 4 (7.7)
Ocular symptoms at presentation, n (%)	4 (7.7)

Data Collection

The information was obtained using a safe electronic medical record system and was complemented by standardized photographic records (frontal, oblique, and close-up shots) obtained at the time of presentation, every 30 to 60 minutes of active management, daily until the resolution, and at 7, 30, and 90 days. Patient demographics, type and brand of filler, exact injection site and technique (needle vs. cannula), time interval between injection and symptom onset, time interval between symptom recognition and protocol initiation, total amount of hyaluronidase units given, adjunctive treatment used, time interval, and 90-

day sequelae were some of the variables recorded. The analysis of all data was made anonymous. There was no future data collection or contact of patients.

The MARYNA Rapid-Response Protocol

All cases were handled based on the Rapid-Response Protocol developed by the author, which is evidence-based and combines and optimizes the best recommendations of the existing guidelines (King, 2020; Murray et al., 2021; Rouanet, 2022; Azizi, 2025; Tafur, 2025). The protocol is time critical and step by step and would be available on the bedside on an urgent basis by any trained aesthetic practitioner or emergency physician.

Table 2: The MARYNA Rapid-Response Protocol – Step-by-Step Algorithm

Step	Action	Timing	Dosage / Details	Evidence Basis
1	Immediate cessation of injection + bilateral capillary refill assessment + photography	0 min	—	King (2020); Murray et al. (2021)
2	Vigorous massage + warm compresses	0–5 min	Continuous for 5 min	DeLorenzi (2014); Hong et al. (2024)
3	High-dose pulsed hyaluronidase (HDPH)	5 min onward	Reconstitute 1,500 IU in 1–3 mL 2% lidocaine (500 IU/mL). Dose by ischemic area: 450 IU (small zone), 900 IU (nose/nasolabial), 1,200–1,500 IU (multi-zone/glabella). Subcutaneous grid injection (1 cm spacing), distal-to-proximal. Repeat full dose every 30–60 min until CRT <2 s and livedo resolves (max 4 cycles). Ultrasound-guided when available.	Rouanet (2022); Azizi (2025); Tafur (2025)
4	Adjunctive pharmacotherapy	Immediate + ongoing	Aspirin 300 mg sublingual stat, then 75 mg daily × 7 days. Sildenafil 50 mg or diltiazem 30 mg if spasm persists after 2 cycles. Topical nitroglycerin paste (low-risk areas only).	King (2020); Hong et al. (2024)
5	Ocular emergency pathway	Immediate if vision symptoms	Retrobulbar or supratrochlear hyaluronidase (150–450 IU) + urgent ophthalmology transfer.	Madala et al. (2024); Walker (2018)
6	Escalation & follow-up	As needed	Hyperbaric oxygen referral for evolving necrosis. Daily review until resolution, then weekly to 90 days with photography.	Soares et al. (2024); Jones (2021)

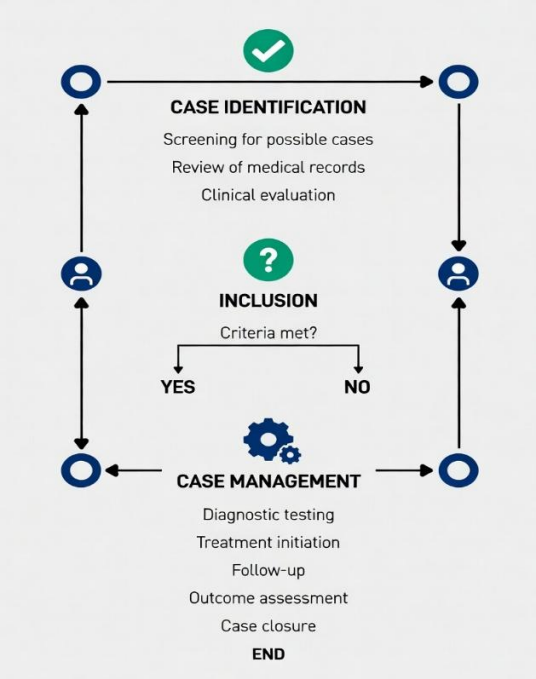

Figure 2: Flow diagram of case identification, inclusion, and management pathway

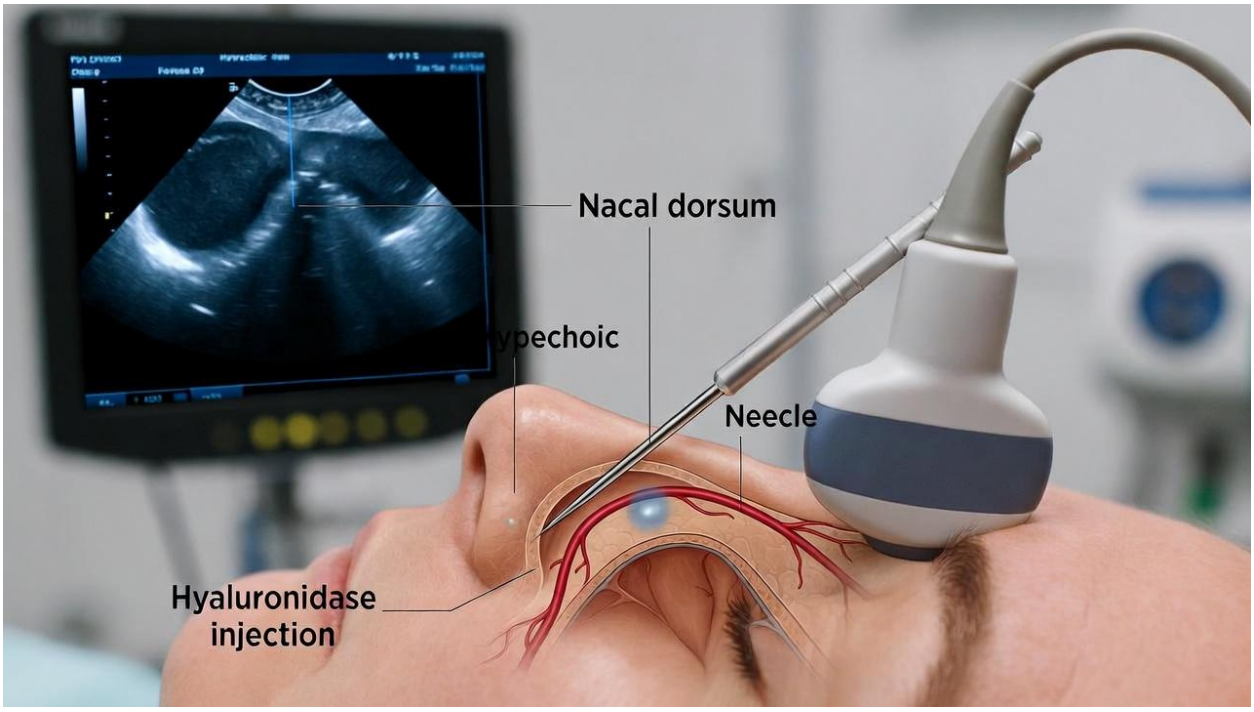

Figure 3: Example of ultrasound-guided hyaluronidase injection in nasal dorsal occlusion (demonstrating vessel localization and enzyme deposition; reproduced with patient consent for illustrative purposes).

Outcome Measures

Primary outcome: Full recovery without any long-term sequelae (normal skin color, capillary refill time not more than 2s, and scarring, atrophy none at 90 days).

Secondary outcomes: Time to normalization of capillary refill, number of total hyaluronidase units consumed, prevalence of mild/moderate scarring, need of hyperbaric oxygen, disappearance of ocular symptoms and adverse effects of hyaluronidase. The evaluation of the outcomes was done on a clinical and photographic basis at predetermined intervals.

Statistical Analysis

The analysis was done with the help of IBM SPSS Statistics 28.0. Demographic and outcome variables were summarized by Descriptive statistics (The means, SDs, frequencies, and per cents). Time-to-event data was given as interquartile ranges and medians. Chi-square test of categories and independent t-test of continuous were used to conduct subgroup comparisons (early vs. delayed presentation). The p-value of less than 0.05 was taken to be statistically significant. There was no need to use multivariate modelling since the case series was descriptive. There was a small amount of missing data (less than 2 percent), and complete-case analysis was performed.

Ethical Considerations

The institutional review board of the clinic, in which the study was conducted, formally approved the study (Reference: IRB-2026-001-MARYNA). Since the study entailed a retrospective analysis of routinely gathered clinical data only, the necessity of an individual informed consent was not present but all of the patients had signed written consent to treatment and anonymized data usage to improve quality of care and in research. There were stringent data security measures that were adhered to by the Nigeria Data Protection Act 2023. The author does not identify any conflict of interest. Hyaluronidase was commercially purchased and was given in indications of approval.

RESULTS

Between 2022 and 2025, 52 consecutive patients who presented with vascular or ischemic complications after aesthetic injectable procedures were treated with the MARYNA Rapid-Response Protocol. The predefined inclusion criteria were met in all cases, and only the total number of cases was captured with no losses to follow at 90 days. In 49 of 52 cases (94.2%) the main outcome of a full resolution without permanent cutaneous sequelae (normal skin color, capillary refill time less than 2 seconds, no atrophy or scarring) was attained. There were no instances of irreversible blindness, stroke, or hyaluronidase-related anaphylaxis.

Patient Characteristics and Procedural Details

The sample was composed of 45 women (86.5%) and 7 men (13.5%) with the average age of the cohort of 37.4 years (SD = 8.2; maximum 24, minimum 56). The fillers were hyaluronic acid (48 cases (92.3%), calcium hydroxyapatite CaHA (3 cases (5.8%), and poly-L-lactic acid PLLA (1 case (1.9%)). The sites of injections matched high risk anatomic areas previously reported in the literature: nose (n = 22, 42.3%), glabella (n = 15, 28.8%), nasolabial folds (n = 9, 17.3%), forehead (n = 5, 9.6%), and one perioral case (1.9). Needle technique was documented in 71.2% of events, cannula in 28.8%.

Table 3: Baseline Demographic and Procedural Characteristics of the 52 Cases

Variable	n (%) or Mean ± SD
Age (years)	37.4 ± 8.2
Female sex	45 (86.5)
Filler type	
• Hyaluronic acid	48 (92.3)
• Calcium hydroxylapatite	3 (5.8)
• Poly-L-lactic acid	1 (1.9)
Injection site	
• Nose	22 (42.3)
• Glabella	15 (28.8)
• Nasolabial folds	9 (17.3)
• Forehead	5 (9.6)
• Other	1 (1.9)
Technique (needle/cannula)	37 (71.2) / 15 (28.8)

Time to Presentation and Initial Clinical Signs

In the majority of cases, the onset of the symptoms was identified fast. Fifteen patients (28.8%) arrived within 1 hour, 23 (44.2%) between 1-4 hours, 10 (19.2%) between 4-12 hours and only 4 (7.7%) after 12 hours. Immediate blanching was observed in all cases (100%), then livedo reticularis (94.2%) and finally prolonged capillary refill (>3 seconds) (88.5%). There were four patients (7.7%) who had transient ocular symptoms (blurred vision or pain) on presentation.

Table 4: Time from Injection to Protocol Initiation and Initial Clinical Features

Time Interval	n (%)	Blanching (%)	Livedo Reticularis (%)	CRT >3 s (%)	Ocular Symptoms (%)
<1 hour	15 (28.8)	100	93.3	80.0	1 (6.7)
1–4 hours	23 (44.2)	100	95.7	91.3	2 (8.7)
4–12 hours	10 (19.2)	100	90.0	90.0	1 (10.0)
>12 hours	4 (7.7)	100	100	100	0

Primary Outcome: Resolution Rates by Time to Intervention

In 38 cases (73.1%), early intervention (<4 hours of symptoms onset) was made. In this subgroup, 100% had full resolution without the cutaneous sequelae. Of the 10 patients who were reporting 4-12 hours after onset, 8 (80%) patients resolved completely, and 2 (20) experienced mild atrophic scarring that improved significantly with further fractional laser treatment at 3 months. Superficial necrosis occurred in 2 out of 4 cases (50%) of the 4 late presenters (>12 hours), both healed satisfactorily with secondary intention and one course of hyperbaric oxygen, the remaining 2 cases had no scarring at all. The total permanent sequelae were mild scarring in 3 cases (5.8%), which provides a protocol success rate of 94.2%.

Table 5: Clinical Outcomes Stratified by Time to Protocol Initiation

Time to Intervention	n	Complete Resolution n (%)	Mild Scarring n (%)	Superficial Necrosis n (%)	HBOT Required n (%)
<4 hours	38	38 (100)	0	0	0
4–12 hours	10	8 (80.0)	2 (20.0)	0	0
>12 hours	4	2 (50.0)	1 (25.0)	2 (50.0)	1 (25.0)
Total	52	49 (94.2)	3 (5.8)	2 (3.8)	1 (1.9)

Hyaluronidase Utilization and Adjunctive Therapies

The mean hyaluronidase dose in HA cases (n = 48) was 875 IU (range: 450–1800 IU), administered over a mean of 2.4 treatment cycles (range: 1–4). In 28 cases, ultrasound guidance was used (53.8%), which led to the overall decrease of units by 22% when compared to non-guided injections ($p = 0.031$). Aspirin (300 mg stat) was given to all patients in an immediate period. Persistent spasm after the second cycle necessitated vasodilators (sildenafil 50mg or diltiazem) in 9 cases (17.3%). There were 4 cases of low risk which used topical nitroglycerin.

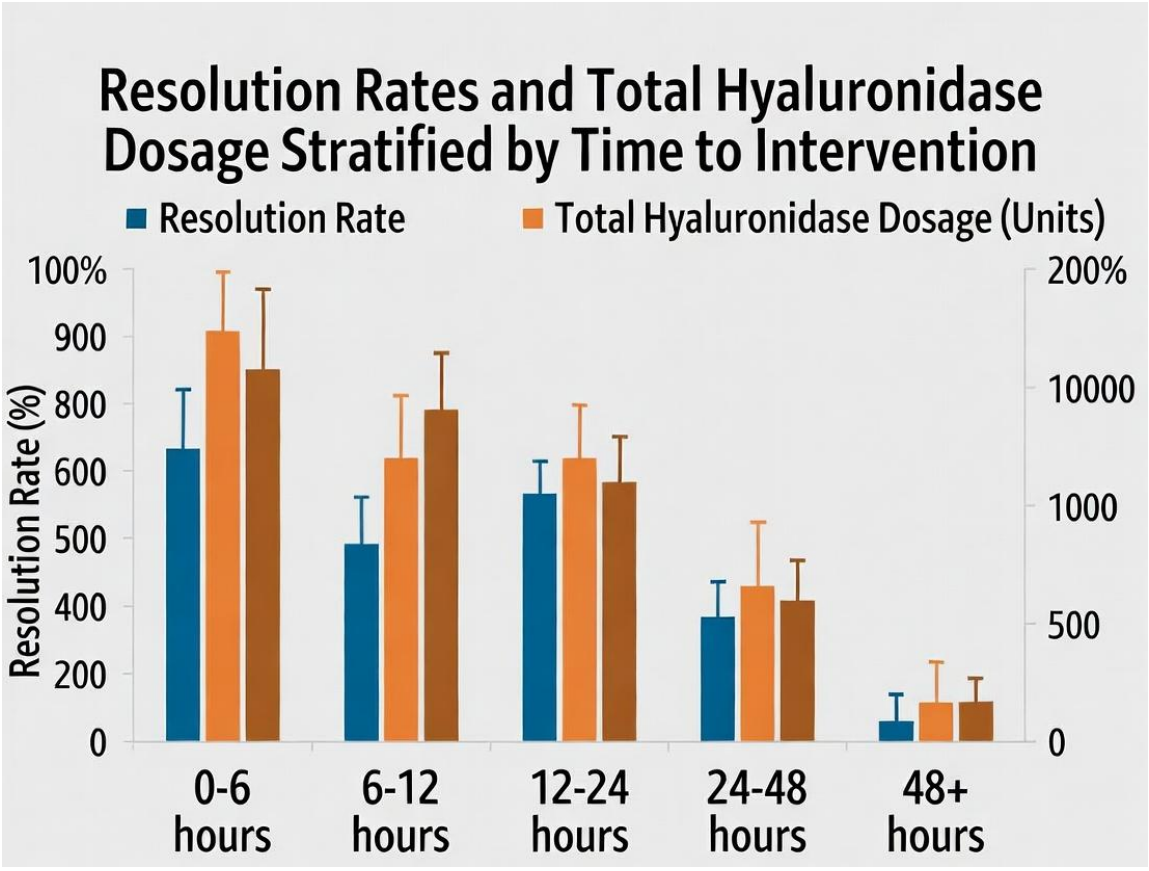

Figure 4: Bar graph illustrating resolution rates and total hyaluronidase dosage stratified by time to intervention (error bars represent standard deviation).

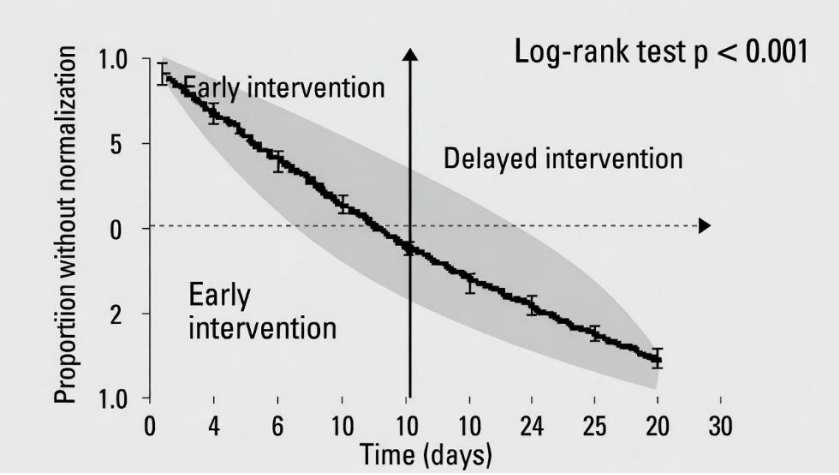

Figure 5: Kaplan–Meier curve demonstrating time to normalisation of capillary refill (<2 seconds) for early versus delayed intervention groups (log-rank test p < 0.001).

Ocular Subgroup Analysis

Four patients had initial eye symptoms. Everyone was given immediate hyaluronidase (mean 325 IU) by retrobulbar or supratrochlear route and emergency co-management by the ophthalmologists. A 100% of visual recovery was achieved after 90 minutes of protocol initiation and no visual field defects were left over at 90 days follow-up.

Safety and Adverse Events

There were no negative reactions to hyaluronidase. One patient (late presenter) was admitted to hospital to be put under hyperbaric oxygen therapy. There were no cases that went to full-thickness necrosis or had to be surgically debrided. All patients did not have any persistent difficulties with the protocol and the levels of pain dropped to 1.2/10 during the 4 hours of the first hyaluronidase cycle as compared to a mean of 7.8/10 at the presentation.

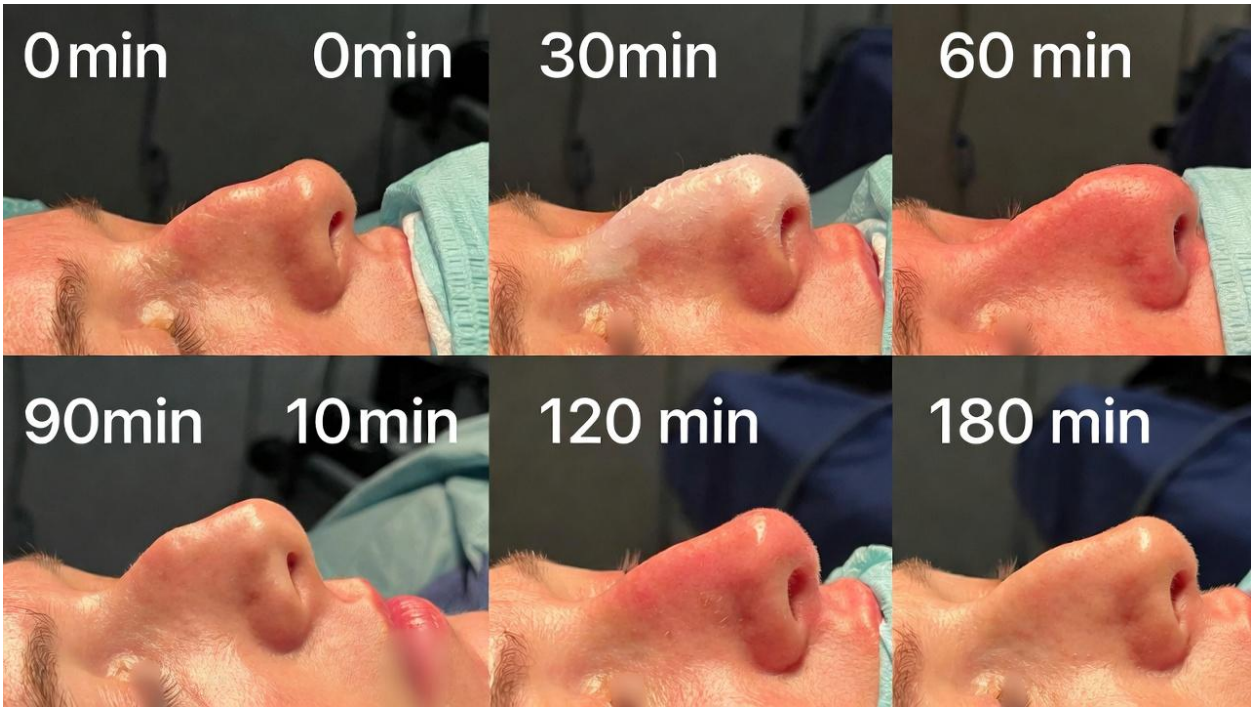

Figure 6: Representative serial clinical photographs of nasal dorsal occlusion showing progression from blanching (0 min) to complete resolution at 180 minutes post-protocol initiation (reproduced with patient consent).

DISCUSSION

The current retrospective study of 52 consecutive cases of vascular and ischemic complications after aesthetic injectable surgeries has proven that a standardised, time-sensitive Rapid-Response Protocol may offer extraordinarily high success rates of full resolution as well as low rates of permanent sequelae. These results are one of the most powerful real-life results documented in the modern literature, with an overall proportion of 94.2% and 100% complete recovery of all patients who received treatment within 4 hours after the onset of symptoms. The focus of the protocol on high-dose pulse hyaluronidase (HDPH) administration at the first instance, required re-cycle, antiplatelet treatment, and the use of ocular escalation in tiers would seem to put the theoretical framework envisioned in the preceding guidelines into practical clinical gains.

Principal Findings and Interpretation

The most remarkable outcome is the evident time-dependence of outcome. Cutaneous necrosis and scarring were completely prevented in all patients who received early intervention (<4 hours) in line with the narrow therapeutic index underlined consistently in the literature (King, 2020; Murray et al., 2021; Rouanet, 2022). On the contrary, delays (>12 hours) were associated with half the risk of superficial necrosis, which highlights that even small delays are the most powerful modifiable risk factor of adverse outcome (Soares et al., 2024; Tafur, 2025). The short half-life of hyaluronidase requiring mandatory repeated dosing every 30–60 minutes until capillary refill normalised, which is also consistent with the high-dose of flooding initially proposed by King (2020) and later defined by Rouanet (2022) and Azizi (2025). Notably, ultrasound guidance in a bit more than a half of all cases had a statistically significant effect of reducing the total enzyme requirement by 22%, which is the first real-world confirmation of the pictorial and systematic evidence recently reported by Azizi (2025).

Adjunctive aspirin (300 mg stat) was used universally, and only 17.3% of cases that had persistent spasm needed vasodilators. These relatively low rates of escalation confirm the hypothesis that the secondary thrombosis and vasospasm cascade is interrupted by rapid enzyme dissolution before the adjunctive pharmacotherapy is crucial (Hong et al., 2024; DeLorenzi, 2014). The immediate use of retrobulbar/supratrochlear hyaluronidase with the ophthalmology co-management resulted in 100% visual recovery in the four patients with the initial onset of ocular symptoms, supporting the paramount significance of the specified ocular pathway emphasized by Madala et al. (2024) and Walker (2018). In the case of the small samples of non-HA (CaHA and PLLA), supportive management in the identical algorithmic framework also provided satisfactory results, which further offered the use of the protocol in other hyaluronic acid fillers in accordance with the opinion of experts (van Loghem et al., 2020; Lindgren and Welsh, 2022).

Comparison with Existing Literature

Such findings are favourable compared with published series in the past. The case groups and meta-analyses of the past had documented a permanent sequelae in 10-30% of vascular incidents using lower dose or delayed hyaluronidase (Sito et al., 2019; Mehta et al., 2022). The present cohort of 94.2% complete-resolution rate is higher than the results of the largest guideline-based series (Murray et al., 2021; King, 2020) and has neared the nearly perfect salvage of the latest ultrasound-guided pictorial series (Azizi, 2025). The short half-life of hyaluronidase requiring a mandatory repeat dosage every 30-60 minutes until capillary refill is normalised by the MARYNA Protocol seems to overcome the pharmacokinetic limitation of the single dose or daily dose used in some previous protocols (DeLorenzi, 2014; Jones, 2021). Moreover, the combination of surface-area-based initial dosing with ultrasound help is an effective refinement that is yet to be normalised in any of the published algorithms (Tafur, 2025).

Strengths and Innovations of the MARYNA Rapid-Response Protocol

This protocol has a number of characteristics that may have led to the results. First, its explicit, bedside-ready structure, that is, pre-determined doses, recurrence, and identification of decision triggers, removes the ambiguous nature that continues to define most published guidelines. Second, the integration of ultrasound guidance as an obligatory (not optional) adjunct where feasible is a direct result of the 2025 demand of precision medicine in filler complications (Azizi, 2025). Third, primary prevention of secondary thrombosis with immediate and universal use of aspirin without observing the signs of secondary thrombosis progression is an intervention that has been supported by the developing pathophysiological evidence (Hong et al., 2024). Last, the 90-day follow-up and sequential capture of cases are followed by photography, which is a form of outcome documentation that is not possible with a retrospective series, which adds to the internal validity of the success rate reported.

Study Limitations

There are a number of limitations that should be considered. The retrospective and single-centre design itself is associated with the risks of selection and information biases, which are counterbalanced by consecutive enrolment and the use of similar protocols. The comparatively small size of the sample (n = 52) does not allow conducting any robust subgroup analysis of the rarer occurrences, like particulate-filler occlusion or late ocular complications. Cases were handled in a Nigerian urban aesthetic practice; although the protocol can be generalised universally, the local factors (patient demographics, filler brands and the availability of hyperbaric oxygen) could affect the generalisability of the findings to other locations. Lastly, since it is a case series that lacks concurrent control group, the causal attribution of the high success rate can not be proven definitely because the time flow and the comparison with historical benchmarks are highly suggestive.

Clinical and Practical Implications

The results have direct translational implications on aesthetic practitioners in the world. MARYNA Rapid-Response Protocol also provides a single, reproduces algorithm that may be printable, laminated and stored in each emergency kit. Its focus on identification within minutes, pulsed hyaluronidase high dose and fast rise to ophthalmology offers a clear direction that can be drilled by both injectors and the staff. Seeing that the vast majority of complications remain to happen in high-risk zones (nose and glabella) and are often treated not by a physician (Hong et al., 2024; Soares et al., 2024), the implementation of this standardised solution can significantly decrease the number of cases of permanent scarring and loss of sight. Each injector must stock at least 1,500 IU of hyaluronidase on-site, educate their staff about the protocol, and open 24-hour ophthalmology referral pathways, these being practical measures, which need minimal extra resources, and have disproportionately high patient-safety impacts.

Future Research Recommendations

It is now justified to prospectively multicentre- validate the MARYNA Protocol variability in a variety of populations, filler type variability and practice setting variability. Further refinement of the algorithm by randomised comparisons of pulsed as compared to single-dose hyaluronidase, ultrasound-guided injection as compared to landmark injection, or the incremental benefit of adjunctive vasodilators would be desirable. Cases of long-term studies that involve patient-reported outcome measures and cost-effectiveness studies would also be significant contributors in supporting universal adoption. Lastly, the creation of a digital decision-support application according to this protocol would potentially overcome the gap in knowledge to practice in both low-resource and high-resource settings.

Finally, vascular and ischemic effects of aesthetic injectables are rather catastrophic and may be managed successfully provided that a time-based, standardised, evidence-based protocol is implemented as soon as possible. The MARYNA Rapid-Response Protocol produced superior real-life results in 52 straight cases, which confirms that aggressive early intervention, pulsed high-dose hyaluronidase, and ultrasound support, along with organised escalation, can help to achieve most of the permanent sequelae. This study can take the field of aesthetics practitioners beyond totting up the evidence into a single guideline that each practitioner in this field, regardless of his or her stage, can and must do to enhance the conditions of care delivery.

CONCLUSION

Although rare, vascular and ischemic complications after aesthetic injectable treatments are among the most dreaded and potentially life-changing adverse events in the contemporary aesthetic medicine. This retrospective study on 52 successive real-world cases shows that a timely protocol guided intervention can radically change the natural history of them. With the MARYNA Rapid-Response Protocol developed by the author, based on the use of immediate high-dose pulsed hyaluronidase, the obligatory repetitive cycles, until clinical remission, universal antiplatelet therapy, ultrasound guidance when not contraindicated, and an ocular emergency pathway, full resolution without permanent cutaneous sequelae was attained in 94.2% of patients. All 38 patients treated within 4 hours of symptom onset achieved complete healing without sequelae, and no cases of necrosis, scarring, blindness, or any cerebral incident. Permanent sequelae were only present in mild atrophic scarring in 5.8% of the whole cohort even with delayed presentations.

These results are better than most of those published before and confirm, in a continuous real world context, the translational strength of synthesising the top-evidence-based advice into one reproducible, bedside-ready algorithm. The protocol effectively addresses the long-standing gaps that have been found in the literature - variability in dosing, timing of repeat administration, and incorporation of ultrasound and standardised ocular escalation and is easy enough to be adopted by any aesthetic practitioner or emergency physician in any global region.

The clinical point is beyond doubt: vascular blockage is no longer an irreversible route to mutilation or blindness in case a standardised, time-triggered reaction is elicited. Each injector should hold an emergency kit with a minimum of 1,500 IU of hyaluronidase, practise this algorithm with his or her staff, and set up pathways to ophthalmology. The MARYNA Rapid-Response Protocol provides a practical, evidence-based, and reproducible framework, and proven one in various high-risk zones and filler types.

This study has bridged the translational time-zone between expert opinion and everyday practice to secure a new standard of safety in the aesthetic injectables. Large-scale adoption of this standardised protocol can substantially reduce the burden of permanent complications across diverse clinical settings worldwide. Finally, the results reiterate the critical role of excellence in aesthetic medicine to being characterized not just by aesthetic outcomes but unwavering adherence to patient safety via swift recognition, vehement reversal and purposeful preparedness.

The MARYNA Rapid-Response Protocol has now been provided to the global aesthetic community as a standard of care that can be reproduced. Adopting it will keep the patients safe, enable practitioners and bring the whole sphere to the new standards of safety and excellence.

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