

LATE COMPLICATIONS ASSOCIATED WITH THE USE OF HYALURONIC ACID DERMAL FILLERS IN FACIAL AESTHETIC PROCEDURES: AN INTEGRATIVE REVIEW

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ABSTRACT

The use of hyaluronic acid dermal fillers has become increasingly prominent in facial aesthetics due to their effectiveness and safety profile. However, late complications associated with these procedures have been increasingly reported in the scientific literature. This study aimed to analyze the scientific evidence regarding the main late complications related to facial hyaluronic acid fillers. An integrative review was conducted using PubMed/MEDLINE, SciELO, and BVS databases, including studies published between 2017 and 2026. The findings demonstrated that intermittent delayed edema, inflammatory nodules, granulomas, hypersensitivity reactions, and biofilm-associated complications are the most frequently reported adverse events, being associated with technical factors, biomaterial characteristics, and systemic patient conditions. It is concluded that preventing such complications requires careful clinical assessment, comprehensive anatomical knowledge, and early management strategies, contributing to greater patient safety and improved aesthetic outcomes.

Keywords: Adverse complications, Dermal fillers, Facial aesthetics, Hyaluronic Acid, Patient safety.

INTRODUCTION

Facial aging is a multifactorial process characterized by progressive loss of soft tissue volume, laxity of ligamentous structures, facial bone remodeling, and changes in adipose compartments. Among the most affected regions is the midface, particularly the anteromedial cheek, areas that are responsible for maintaining facial symmetry, harmony, and a youthful appearance. In this context, hyaluronic acid-based fillers have been widely used in facial aesthetics because of their ability to provide volumization, tissue support, and rejuvenation through a minimally invasive technique.¹ The use of hyaluronic acid has gained increasing prominence in recent years due to the high demand for nonsurgical aesthetic procedures, greater emphasis on physical appearance, the desire to achieve a more youthful appearance, and advances in facial harmonization techniques. In addition to its high biocompatibility and resorbable nature, hyaluronic acid has clinical safety, which favors its use in different anatomical regions of the face. However, despite its aesthetic and functional benefits, complications associated with facial fillers have been increasingly reported in the scientific literature.^{1,2}

Complications resulting from the use of hyaluronic acid-based fillers may range from mild and transient manifestations, such as edema, erythema, bruising, and local pain, to severe manifestations, including infections, nodule formation, granulomas, tissue necrosis, and vascular occlusion. Among these, vascular obstruction stands out because of the possibility of rapid progression to ischemia, skin necrosis, and even irreversible visual loss.^{2,3,4} The occurrence of these complications is related to factors such as inadequate technique, lack of anatomical knowledge, incorrect product selection, and performance of the procedure by unqualified professionals.² In this context, there is considerable concern among the scientific community and professionals working in aesthetics regarding the safety of injectable aesthetic procedures and the need for continuous professional updating. Recent studies have investigated the main pathophysiological mechanisms related to hyaluronic acid complications, as well as preventive strategies and therapeutic protocols for the early management of these adverse events. In addition, the marked increase in demand for facial harmonization reinforces the importance of adopting measures that ensure greater patient safety.²

Therefore, it is relevant to gather and analyze the available evidence in the literature regarding complications associated with facial filling using hyaluronic acid. Thus, through an integrative review, this study aims to identify the main complications related to the use of hyaluronic acid in facial aesthetics, their predisposing factors, clinical manifestations, prevention methods, and therapeutic possibilities based on the literature.

OBJECTIVES

To analyze, through an integrative literature review, the available scientific evidence regarding complications resulting from hyaluronic acid fillers in facial aesthetics. Specifically, the study aims to identify predisposing and risk factors, clinical manifestations and the frequency of these adverse events, preventive methods, and the therapeutic approaches described, with the purpose of supporting safer and more effective practices in facial harmonization.

METHODS

This integrative review followed Ganong's methodological framework, organized into six stages: selection of the topic and research question, establishment of inclusion and exclusion criteria, definition of the information to be extracted, evaluation of the studies, interpretation of the results, and presentation of the review. The guiding question, structured according to the PICO strategy, was: "What are the main late complications and safety outcomes associated with the use of hyaluronic acid fillers in facial procedures, according to the current literature?"

The data search was conducted in May 2026 in the PubMed/MEDLINE, SciELO, and VHL databases. The Medical Subject Headings (MeSH Terms) and Health Sciences Descriptors (DeCS) were used for vocabulary control and identification of corresponding terms. The search string combined the terms ("Hyaluronic acid" OR "Ácido Hialurônico") AND ("Dermal Fillers" OR "Preenchedores Dérmicos") AND ("Postoperative Complications" OR "Complicações Pós-Operatórias" OR "Delayed-onset edema") AND ("Face") using the Boolean operators OR and AND.

The inclusion criteria comprised original articles, case reports, and consensus statements published between 2017 and 2026 in Portuguese, English, or Spanish. Selection was performed by two independent researchers to avoid bias, resulting in a final corpus of 7 articles. Data analysis was performed narratively,

correlating complications such as inflammatory nodules and intermittent delayed edema with new clinical triggers, such as the use of GLP-1 analogues and innovations in hybrid fillers.

RESULTS

The integrative analysis of the seven included articles allowed a comprehensive characterization of late complications associated with the use of hyaluronic acid fillers in facial aesthetic procedures, as well as the identification of emerging predisposing factors and contemporary prevention and management strategies.

Table 1: Characteristics of the included studies.

Author and year	Methodologic Design	Population/ Sample	Main Focus	Main Findings	Level of Evidence
Piton et al. (2025)	Systematic Literature Review	Analysis of multiple studies on filler complications	Taxonomy and classification of late complications	Identification of 8 main categories of late complications; intermittent delayed edema and inflammatory nodules as the most frequent	II
Ciaramicolo et al. (2024)	Case Report	3 patients undergoing semaglutide (Ozempic®) therapy	Association between GLP-1 analogues and delayed facial edema after filler injection	Recurrent intermittent facial edema in patients using GLP-1; hypothesis of systemic inflammatory modulation as the mechanism; absence of technical or biomaterial failure	IV
Urdiales Galvez et al. (2017)	Expert Consensus	Panel of 15 specialists in facial aesthetics	Recommendations for the prevention of technical complications	Anatomical knowledge, safe injection technique, appropriate product selection, and injector experience as pillars of prevention; standardized technical safety protocols	III

Lee et al. (2026)	Prospective Controlled Study	120 patients; 24-week follow-up	Safety and efficacy of hybrid fillers (hyaluronic acid + polynucleotides)	Favorable tolerability profile; absence of serious adverse events; maintenance of volume and patient satisfaction; no stratification regarding systemic medications	II
Qiu et al. (2026)	Retrospective Study	85 patients receiving combined treatments	Efficacy of combined treatments (hyaluronic acid + other bioactive agents) for photoaging	Synergy between different bioactive agents; dynamic interaction between components determines final safety; importance of considering biomaterial-host compatibility	III
Bettiol et al. (2026)	Longitudinal Observational Study	60 patients; 12-month follow-up	Orofacial function and quality of life after facial filler treatment	Preservation of masticatory and phonatory function in most cases; impact on quality of life correlated with functional maintenance, not only with the absence of complications;	II
				delayed edema significantly affects function	

Shturman et al. (2026)	Review of Minimally Invasive Treatments	Analysis of 12 corrective protocols	Minimally invasive approaches for correction of aesthetic complications	Importance of individualized management; integration of energy-based technologies; consideration of the “corrective patient archetype”; psychosocial safety as a component of success	III
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Source: Prepared by the authors (2026).

The results of this integrative review demonstrate a clear evolution in the understanding of late complications associated with hyaluronic acid fillers. First, a spectrum of manifestations extending beyond mere local inflammation has become established, including intermittent delayed edema, inflammatory nodules, foreign-body granulomas, conditions suggestive of biofilm formation, and delayed hypersensitivity reactions. It is important to emphasize that these events affect not only morphological aspects but also orofacial function and psychosocial well-being, with a direct impact on the patient’s quality of life—a dimension intrinsic to the contemporary concept of safety.

At the same time, traditionally emphasized risk determinants—such as gaps in anatomical knowledge, inadequate technique, inappropriate product selection, and injector inexperience—remain relevant but do not fully explain the heterogeneity of outcomes. Recent literature introduces systemic risk modifiers, particularly the use of GLP-1 agonists and other drugs with the potential to modulate inflammation, which may alter the tissue response to the biomaterial and thereby predispose patients to complications with delayed onset and an intermittent course. Regarding biomaterials, studies involving hybrid formulations support a favorable safety profile in general populations but suggest individual variability that remains insufficiently characterized. This dissociation—positive overall safety versus idiosyncratic responses in subgroups—reinforces the need for prior risk stratification that considers not only the product and technique but also the patient’s systemic status and concomitant therapies.

DISCUSSION

The results of this study demonstrate that late complications associated with the use of hyaluronic acid fillers in facial aesthetic procedures represent a multifactorial phenomenon, whose understanding requires the integrated synthesis of technical, biomaterial, systemic, and psychosocial knowledge. While previous studies focused primarily on technical-procedural factors as the sole determinants of safety, contemporary literature reveals that the heterogeneity of clinical outcomes emerges from dynamic interactions among multiple levels of factors.

Overview of Late Complications in Facial Filling with Hyaluronic Acid

The analysis of the included studies allows the characterization of a broad spectrum of late

complications occurring weeks to months after the initial procedure. Unlike acute complications, such as vascular occlusion or necrosis, which manifest immediately and are primarily attributable to technical error, late complications exhibit a distinct phenomenological pattern. Intermittent delayed facial edema emerges as the most frequently reported complication, characterized by recurrent episodes of swelling that resolve spontaneously between events. Inflammatory nodules and foreign-body granulomas constitute the second most common category, frequently associated with delayed hypersensitivity reactions or bacterial biofilm formation. The clinical importance of this categorization lies in the fact that each type of complication involves a distinct pathophysiological mechanism and, consequently, a different therapeutic strategy. The temporal pattern of late complications suggests that they do not represent primary tissue injury, as expected in acute technical complications, but rather recurrent inflammatory decompensation or failure of biomaterial integration over time. This observation is fundamental for understanding the predisposing factors discussed in the following section.³

Predisposing Factors and New Clinical Triggers — The Influence of Systemic Conditions on the Safety of Facial Fillers

To adequately answer the guiding question of this review — “What are the main late complications and safety outcomes associated with the use of hyaluronic acid fillers in facial procedures?” — it is not sufficient merely to identify the complications; it is necessary to understand the predisposing mechanisms that explain why some patients develop these complications while others undergoing technically similar procedures do not. The expert consensus by Urdiales-Gálvez et al.² is based on the premise that complications of facial fillers arise primarily from insufficient anatomical knowledge, inadequate injection technique, inappropriate product selection, and lack of injector experience. This technically centered paradigm was, and remains, entirely valid for acute complications and many early complications. However, it has an important explanatory limitation when confronted with contemporary findings. The case report by Ciaramicolo et al.⁴ documents a remarkable finding: intermittent delayed facial edema after hyaluronic acid filler injection in patients receiving semaglutide (Ozempic®), a widely prescribed GLP-1 receptor agonist. What makes this case clinically significant is not the complication itself, but the context in which it occurred: a procedure performed by an experienced professional, with an appropriate injection technique and suitable product, and without vascular injury or technical failure. In other words, all the technical predisposing factors identified by Urdiales-Gálvez et al.² as causal were absent or optimized, yet the complication still occurred. This phenomenon suggests the existence of a new class of predisposing factors not contemplated by the technical paradigm of 2017.

Ciaramicolo et al.⁴ propose that the common factor among their patients — semaglutide therapy — acts as a systemic modifier of the inflammatory response. Although the report does not provide its own mechanistic data, the hypothesis is based on well-characterized properties of GLP-1 agonists: reduction of systemic inflammatory markers, modulation of the adaptive response, and effects on endothelial permeability. The integrated explanation is that the injected biomaterial, hyaluronic acid, triggers the expected local inflammatory response, which would normally be rapidly resolved by the host's homeostatic systemic inflammatory state. However, in patients receiving GLP-1 analogue therapy, chronic modulation of the inflammatory response may result in a biphasic response: excessive reduction of local inflammation during the initial phase, causing fibrosis or entrapment of the biomaterial, followed by periodic decompensation when systemic inflammatory suppression fluctuates or when local stimuli reactivate inflammation. This mechanism explains why the edema is

intermittent and why it occurs in patients without technical failure.

Integrated analysis with subsequent studies reveals a crucial pattern. The prospective study by Lee et al.¹ evaluated hybrid fillers, hyaluronic acid plus polynucleotides, over 24 weeks and documented a favorable tolerability profile, with no serious adverse events. There is no contradiction with Ciaramicolo et al.⁴, but rather complementarity: Lee et al.¹ confirm that hyaluronic acid, even in new formulations, maintains a favorable safety profile when used in a prospectively monitored general population, whereas Ciaramicolo et al.⁴ demonstrate that biomaterial safety is not equivalent to universal safety across all patient subpopulations. The gap between the two studies is revealing: Lee et al.¹ did not stratify their population according to the use of GLP-1 analogues or other inflammation-modulating drugs. This lack of pharmacological stratification is particularly relevant considering that Lee et al.¹ was published in 2026, a period of increasing GLP-1 use, and that it is plausible that disaggregated data from Lee et al. would reveal safety differences between subgroups with and without GLP-1 use. The retrospective study by Qiu et al.⁵, which investigated combined treatments for photoaging, provides additional important context. Although Qiu et al.⁵ did not specifically investigate late complications, their findings regarding interactions among different bioactive agents reinforce the concept that the final safety of the procedure does not arise from a single isolated component, but from the dynamic interaction among multiple factors. Applying this reasoning to the findings of Ciaramicolo et al.⁴, the complication may be understood as the result of the interaction between hyaluronic acid, as a stimulus for a local inflammatory reaction, and an altered systemic inflammatory state, as a modifier induced by GLP-1. The biomaterial itself remains safe, as documented by Lee et al.¹; decompensation occurs at the interface between local and systemic factors.

Prevention Strategies and Therapeutic Protocols

The literature analyzed demonstrates a clear paradigm shift. The consensus by Urdiales-Gálvez et al.² establishes the fundamental basis for any preventive strategy: in-depth anatomical knowledge of facial vasculature, safe injection techniques, including prior aspiration, use of cannulas in high-risk areas, and slow injection of small volumes, product selection based on rheological properties compatible with the anatomical area, and appropriate patient preparation. These preventive measures centered on technical optimization remain entirely valid and necessary to avoid acute complications and many early complications. However, when technical prevention fails or when late complications occur, the literature points toward a more sophisticated hierarchy of intervention. Management of inflammatory nodules and delayed edema presents an important dichotomy: in cases of suspected bacterial biofilm, the classical approach involves long-term antibiotic protocols, such as macrolides including clarithromycin, although efficacy is often limited by the protective nature of the biofilm matrix. In immune-mediated reactions, including granulomas or inflammatory nodules, treatment involves the use of hyaluronidase to degrade the filler, with or without corticosteroids, either intralesional or systemic, and, in refractory cases, immunomodulatory agents.

The finding by Ciaramicolo et al.⁴ regarding delayed edema associated with the use of GLP-1 analogues adds an important layer of complexity. In patients receiving GLP-1 therapy, administration of hyaluronidase or corticosteroids may require adjustments based on the patient's systemic inflammatory status. Current literature still lacks specific guidelines for this subgroup, representing an important gap to be addressed. The study by Shturman et al.⁶ offers a different perspective by proposing a minimally invasive corrective approach. Rather than aggressive protocols based solely on

chemical degradation with hyaluronidase or systemic suppression with corticosteroids, Shturman et al.⁶ propose individualizing the therapeutic plan not only according to the complication, but also according to the patient profile, including age, previous history, and expectations. The authors suggest that the use of energy-based technologies, such as intense pulsed light, also mentioned by Qiu et al.⁵, may be integrated into complication management, acting on modulation of the local inflammatory response and improving skin quality, thereby assisting in the resolution of late inflammatory conditions. This convergence with the view that complication correction should be integrative marks an important evolution: while Urdiales-Gálvez et al.² focused on “how to inject,” Shturman et al.⁶ focus on “how to manage outcomes holistically.”

Functional Safety and Patient Quality of Life — Beyond the Absence of Complications

The integrative literature review reveals a fundamental paradigm shift that transcends previous technical discussions: the success of a facial filler procedure should not be measured solely by the absence of severe complications, but also by preservation of orofacial function and maintenance of long-term quality of life (QoL). The longitudinal observational study by Bettiol et al.⁷ is central to this discussion. By assessing orofacial function after mandibular angle contouring, the authors challenge the reductionist view that “safety = absence of adverse events.” Safety must include preservation of fundamental functions: mastication, speech, and facial expression. Bettiol et al.⁷ demonstrate that even in technically successful procedures without late inflammatory complications, changes in muscular and ligamentous dynamics may affect orofacial function. If a filler produces an apparently perfect aesthetic result but causes masticatory discomfort or speech alteration, the procedure has failed in one of its primary safety outcomes. This evidence integrates critically with the findings of Ciaramiccolo et al.⁴: intermittent delayed edema is not merely an isolated inflammatory problem; by definition, it is a factor causing recurrent functional impairment that reduces the patient’s quality of life over time. A patient experiencing recurrent episodes of facial edema lives in a constant state of vigilance, with a negative impact on confidence, self-image, and satisfaction with the outcome of the procedure.

The study by Shturman et al.⁶ further expands this discussion by introducing the concept of the “corrective patient archetype” and the psychosocial perspective of safety. Complications such as inflammatory nodules or intermittent edema are not neutral events. They generate anxiety and distress because of their recurrent and unpredictable nature, doubts regarding the choice of professional and product, with consequent loss of trust in the physician-patient relationship, and a direct impact on self-image, since the complication alters the face itself, undermining the very reason why the patient sought the procedure. Shturman et al.⁶ argue that the management of these complications should be holistic: patient safety involves not only clinical resolution but also restoration of confidence and self-image. The “corrective patient” is one who has already had a negative experience and whose safety in future procedures depends on an approach that takes this emotional burden into account.

CONCLUSION

Considering the results of the present integrative review, it can be concluded that late complications associated with the use of hyaluronic acid dermal fillers in facial aesthetic procedures are multifactorial events influenced by injection technique, biomaterial characteristics, individual inflammatory response, and the patient’s systemic conditions. The main adverse events described include intermittent delayed edema, inflammatory nodules, granulomas, delayed hypersensitivity

reactions, and conditions associated with biofilm formation.

Therefore, it is recommended that professionals responsible for injectable aesthetic procedures adopt individualized clinical assessment, in-depth anatomical knowledge, careful product selection, and protocols for the prevention and early management of complications. In addition, further prospective studies with larger numbers of patients and stratification of risk factors are needed in order to improve safety protocols and strengthen evidence-based clinical practice.

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