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REVIEW ARTICLE

FACIAL INJECTABLE FILLERS IN AESTHETIC MEDICINE: A SYSTEMATIC REVIEW OF CLINICAL APPLICATIONS, SAFETY, AND COMPLICATIONS

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Abstract

Background: Facial injectable fillers have become a cornerstone of modern aesthetic medicine, offering minimally invasive solutions for facial rejuvenation, contouring, and volume restoration. Despite their widespread use and generally favorable safety profile, complications ranging from mild local reactions to severe vascular events remain a clinical concern.

Objective: This systematic review aims to evaluate the efficacy, safety, and complication profile of facial injectable fillers, with particular emphasis on risk factors, prevention strategies, and management approaches.

Methods:A systematic review was conducted in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. A comprehensive literature search was performed across PubMed, Scopus, Web of Science, and the Cochrane Library for studies published between 2000 and 2025. Keywords and MeSH terms included “dermal fillers,” “facial injectable fillers,” “hyaluronic acid fillers,” “aesthetic medicine,” and “complications.” Eligible studies included randomized controlled trials, cohort studies, case-control studies, and systematic reviews focusing on facial dermal fillers. Data extraction and quality assessment were conducted using standardized tools, including the Cochrane Risk of Bias Tool and the Newcastle–Ottawa Scale.

Results:A total of 487 records were identified, of which 30 high-quality studies met the inclusion criteria. Hyaluronic acid fillers were the most commonly investigated. Immediate complications such as pain, swelling, and erythema were frequently reported but self-limiting. Early complications included infection and nodules, while late complications such as granuloma formation and filler migration were less common. Severe complications, including vascular occlusion, tissue necrosis, and vision loss, were rare but clinically significant.

Conclusion: Facial injectable fillers are effective and generally safe when administered by trained practitioners. However, the potential for serious complications underscores the importance of anatomical knowledge, proper injection technique, and early recognition and management of adverse events.

Keywords: Facial fillers, Hyaluronic acid, Aesthetic medicine, Safety, Dermal complications,

1.INTRODUCTION

Facial injectable fillers have emerged as a cornerstone of modern aesthetic medicine, offering minimally invasive solutions for facial rejuvenation, contouring, and restoration of soft tissue volume. Over the past two decades, there has been a dramatic increase in the demand for non-surgical cosmetic procedures, with dermal fillers ranking among the most commonly performed interventions worldwide[1–3]. This rise is largely attributed to advancements in biomaterials, improved safety profiles, and growing patient preference for procedures that provide immediate results with minimal downtime[4,5]. Dermal fillers are injectable substances designed to restore volume, smooth wrinkles, and enhance facial contours by compensating for age-related structural changes in the skin and underlying tissues. Facial aging is a multifactorial process involving collagen degradation, elastin loss, fat compartment redistribution, and bone resorption, all of which contribute to visible signs such as wrinkles, folds, and volume loss [6–8].

Fillers address these changes through both volumetric augmentation and, in some cases, stimulation of endogenous collagen production, thereby contributing to a more youthful and harmonious facial appearance [9].

Historically, the use of injectable materials for soft tissue augmentation dates back several decades, evolving from early applications of paraffin and silicone to modern biocompatible and biodegradable agents [10].

Since the approval of the first dermal fillers in the early 1980s, the field has expanded significantly, with the development of multiple filler categories, including hyaluronic acid (HA), calcium hydroxylapatite (CaHA), poly-L-lactic acid (PLLA), and polymethylmethacrylate (PMMA) [6].

Currently, HA-based fillers dominate the global market due to their favorable safety profile, reversibility with hyaluronidase, and versatility in treating various facial regions[11,12]. The global popularity of dermal fillers is reflected in epidemiological data. Millions of procedures are performed annually, with a substantial increase observed over the last decade. For instance, reports indicate a significant rise in filler injections, with millions of treatments performed each year in the United States alone, highlighting their widespread acceptance in aesthetic practice [2,6].

This trend is further supported by increased societal emphasis on youthful appearance, technological innovation, and the expanding role of aesthetic medicine in both clinical and cosmetic settings [4,13].

Dermal fillers are utilized for a wide range of clinical indications, encompassing both aesthetic and reconstructive applications. Aesthetic indications include the correction of nasolabial folds, marionette lines, perioral wrinkles, and tear trough deformities, as well as lip augmentation and facial contouring [7,14]. In reconstructive medicine, fillers are employed in the management of conditions such as HIV-associated facial lipoatrophy, post-traumatic defects, acne scarring, and congenital asymmetries [14,15].

The versatility of fillers allows clinicians to tailor treatments to individual patient needs, enhancing both functional and psychosocial outcomes.

Classification of Facial Fillers

Based on Longevity

- Temporary (6–12 months)
- Semi-permanent (1–2 years)
- Permanent (>2 years)

Based on Composition

- Hyaluronic Acid (HA)
- Calcium Hydroxylapatite (CaHA)
- Poly-L-lactic Acid (PLLA)
- Polymethylmethacrylate (PMMA)
- Autologous fat

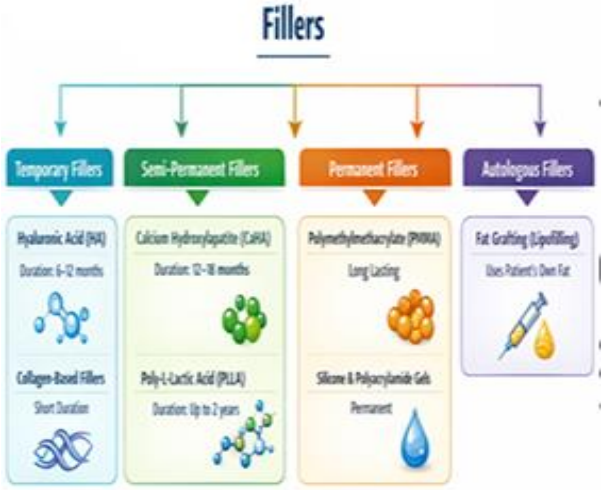

Figure 1. Classification of Facial Fillers

Despite their numerous advantages, the increasing use of dermal fillers has been accompanied by a growing awareness of associated complications. Although most adverse effects are mild and transient, such as swelling, erythema, and bruising, more serious complications, including vascular occlusion, tissue necrosis, and even blindness, have been reported[16–18]. The incidence of complications varies depending on factors such as filler type, injection technique, anatomical site, and practitioner experience[2,17]. Importantly, the rise in complication reports is partly attributable to the increasing number of procedures performed globally, as well as improved reporting systems and clinical awareness [1,16].

The pathophysiology of filler-related complications is complex and multifactorial, involving mechanical, immunological, and infectious mechanisms. For example, vascular occlusion occurs due to embolization or compression of blood vessels, leading to tissue ischemia [16]. Inflammatory and granulomatous reactions may result from foreign body responses or biofilm formation, while infectious complications may arise from contamination during injection or reactivation of latent infections [8,20]. Understanding these mechanisms is essential for both prevention and management of adverse outcomes.

Given the increasing complexity of filler procedures and the diversity of available products, practitioner expertise

plays a critical role in ensuring patient safety. A thorough understanding of facial anatomy, particularly vascular structures, is essential to minimize the risk of complications [11,21]. In addition, appropriate patient selection, proper injection techniques, and adherence to established guidelines are crucial components of safe practice [7,22]. The use of advanced techniques, such as cannula-based injections and ultrasound guidance, has further contributed to improved safety profiles in recent years [6,19].

Another important consideration in the use of dermal fillers is the variability in product characteristics, including rheology, viscosity, elasticity, and degradation rates. These properties influence the clinical behavior of fillers, their longevity, and their suitability for specific indications [11,23]. For instance, highly cross-linked HA fillers provide greater structural support and are preferred for deep volumization, whereas less viscous formulations are used for superficial wrinkle correction [23]. Similarly, biostimulatory fillers such as CaHA and PLLA promote collagen synthesis, offering longer-lasting results compared to purely volumetric agents [6,9].

Ethical and regulatory considerations also play a significant role in the practice of aesthetic medicine. The increasing accessibility of dermal fillers, including their use by non-medical practitioners in some regions, has raised concerns regarding patient safety and the standardization of training[4,24]. Regulatory frameworks vary across countries, emphasizing the need for global consensus on best practices, certification, and quality control in aesthetic procedures [24].

In recent years, there has been a growing emphasis on evidence-based approaches in aesthetic medicine. Systematic reviews and meta-analyses have contributed to a better understanding of filler efficacy, safety, and complication management [2,6]. However, challenges remain due to the heterogeneity of study designs, variations in outcome measures, and the subjective nature of aesthetic assessment [25]. Further high-quality clinical trials are needed to establish standardized protocols and optimize treatment outcomes.

In addition to clinical and technical considerations, patient expectations and psychological factors play a crucial role in the success of filler treatments. Unrealistic expectations, body dysmorphic tendencies, and inadequate patient counseling can lead to dissatisfaction, even in the absence of complications [22,26]. Therefore, effective communication and informed consent are essential components of aesthetic practice.

Looking forward, the field of dermal fillers continues to evolve with ongoing advancements in material science and regenerative medicine. Emerging technologies, including bioengineered fillers, stem cell-based therapies, and combination treatments with platelet-rich plasma (PRP), hold promise for enhancing both safety and efficacy[9,27]. Furthermore, the integration of digital imaging and artificial intelligence in treatment planning may improve precision and personalization in aesthetic procedures [27].

In summary, facial injectable fillers represent a dynamic and rapidly evolving domain within aesthetic medicine. Their widespread use, diverse applications, and generally favorable safety profile make them an indispensable tool for facial rejuvenation and reconstruction. However, the increasing complexity of procedures and the potential for complications underscore the importance of comprehensive knowledge, technical expertise, and adherence to evidence-based practices. This review aims to provide an in-depth analysis of the types, clinical indications, applications, and challenges associated with facial injectable fillers, with a particular focus on complication prevention and management.

2. MATERIALS AND METHODS

2.1 Study Design

This study was conducted as a systematic review following the principles outlined in the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement. The methodology was designed to ensure transparency, reproducibility, and comprehensive identification of relevant literature on facial injectable fillers in aesthetic medicine. The review protocol was developed a priori to minimize bias and guide the systematic selection, extraction, and analysis of data.

2.2 Search Strategy

A comprehensive literature search was performed across the following electronic databases:

- PubMed
- Scopus
- Web of Science
- Cochrane Library

The search encompassed studies published between 2000 and 2025.

Additional filters applied: Language: English Study type: randomized controlled trials, cohort studies, case-control studies, and systematic reviews/meta-analyses Human studies only.

Keywords and Medical Subject Headings (MeSH) terms were applied in various combinations to capture all relevant studies, including:

- "dermal fillers"
- "facial injectable fillers"
- "hyaluronic acid fillers"
- "aesthetic medicine"
- "facial rejuvenation"
- "complications"
- "vascular occlusion"
- "cosmetic procedures"

Boolean operators (AND, OR) were used to refine the search strategy and ensure comprehensive retrieval of relevant literature. Reference lists of included studies and review articles were also screened to identify additional eligible publications.

2.3 Eligibility Criteria

Inclusion Criteria:

- Peer-reviewed articles
- Randomized controlled trials (RCTs), cohort studies, case-control studies, and systematic reviews/meta-analyses
- Studies focusing on facial dermal fillers
- Articles reporting clinical outcomes, indications, or complications
- Publications in English

Exclusion Criteria:

- Non-human studies
- Conference abstracts without full text
- Editorials, letters, and opinion articles
- Studies unrelated to facial applications
- Duplicate publications

2.4 Study Selection Process

All identified records were imported into reference management software, and duplicates were removed. The study selection process was conducted in three sequential stages:

1. **Title screening** – preliminary exclusion of irrelevant studies based on title.
2. **Abstract screening** – evaluation of abstracts for relevance to inclusion criteria.
3. **Full-text review** – detailed assessment for eligibility.

Two independent reviewers conducted all stages of selection. Discrepancies were resolved through discussion or consultation with a third reviewer to ensure objectivity and minimize selection bias.

The study selection process is summarized in a PRISMA flow diagram:

- Records identified through database searching: n = 487
- Records after duplicates removed: n = 420
- Records screened: n = 420
- Full-text articles assessed for eligibility: n = 85
- Studies included in qualitative synthesis: n = 30

This diagram visually demonstrates the rigorous screening and selection process, ensuring transparency and reproducibility of the systematic review (fig. 2).

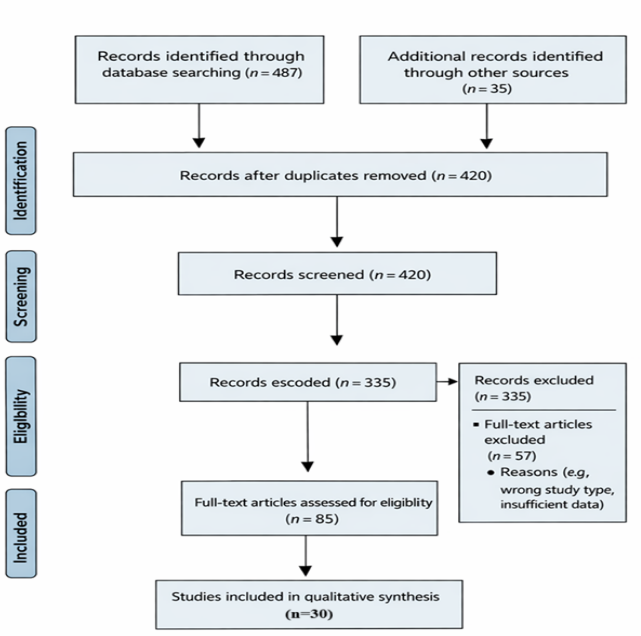

Figure 2. PRISMA Flow Diagram

2.6 Data Extraction

Data extraction was performed using a standardized form to maintain consistency across studies. Extracted variables included:

- Author(s) and year of publication
- Study design
- Sample size
- Type of filler used
- Clinical indications
- Treatment outcomes
- Reported complications
- Follow-up duration

This structured approach facilitated systematic comparison and synthesis of study findings.

2.7 Data Synthesis

Due to heterogeneity in study designs, filler types, outcome measures, and follow-up durations, a quantitative meta-analysis was not feasible. Instead, a qualitative narrative synthesis was performed. Findings were grouped into the following categories:

- Types and classification of fillers
- Clinical indications and applications
- Complications and adverse effects
- Management strategies

This approach allowed for comprehensive integration of diverse evidence while highlighting patterns, trends, and knowledge gaps.

2.6 Quality Assessment and Risk of Bias

The methodological quality of included studies was assessed using validated tools:

- **Cochrane Risk of Bias Tool** for randomized controlled trials (assessing domains such as sequence generation, allocation concealment, blinding, incomplete outcome data, selective reporting, and other sources of bias).
- **Newcastle–Ottawa Scale** for observational studies (assessing selection, comparability, and outcome/exposure domains).

Each study was classified as low, moderate, or high risk of bias. Interpretation of risk-of-bias findings considered the potential impact on reported outcomes:

- **Low-risk studies** provided reliable and internally valid results with minimal influence of confounding factors.
- **Moderate-risk studies** had minor limitations that may slightly affect outcome interpretation but still contributed valuable evidence.
- **High-risk studies** had significant methodological weaknesses that could compromise validity, requiring cautious interpretation of their findings.

Overall, risk-of-bias assessment highlighted the importance of study design, reporting transparency, and methodological rigor in evaluating the safety and efficacy of facial injectable fillers.

Subjective outcomes, such as patient satisfaction and aesthetic improvement, are more susceptible to performance and detection bias due to limited blinding. Despite these limitations, severe complications, including vascular occlusion, tissue necrosis, and visual impairment, were consistently reported across multiple studies and study designs. This consistency suggests that these findings are robust and clinically reliable, even in the presence of methodological heterogeneity.

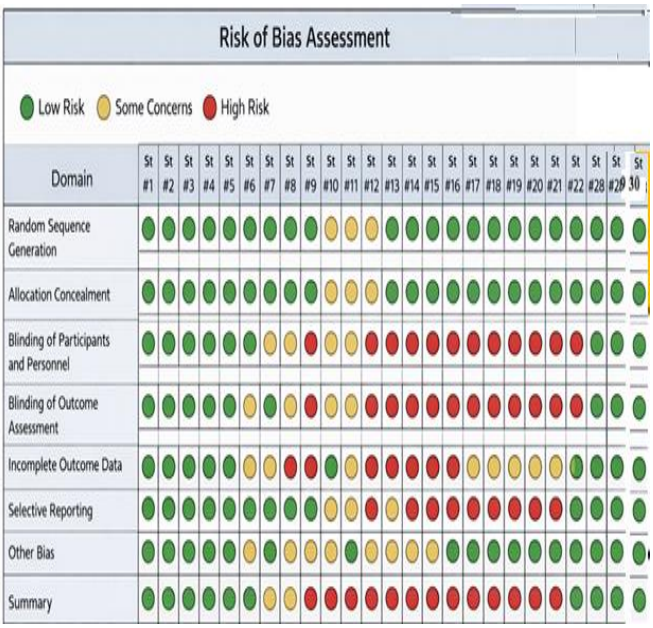

Figure 3. Risk-of-Bias Assessment of Included Studies

Figure 3 presents the risk-of-bias evaluation for the 30 included studies, summarized across key methodological domains. Each study is represented by a column (St #1–St #30), and the domains assessed include: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other sources of bias.

Color coding is used to indicate the level of risk:

- **Green circles:** Low risk of bias
- **Yellow circles:** Some concerns / moderate risk of bias
- **Red circles:** High risk of bias

Furthermore, the convergence of results across RCTs, cohort studies, and systematic reviews strengthens the overall validity of the evidence base, particularly regarding the general safety profile of dermal fillers and the rarity—but clinical significance—of severe adverse events. These improvements are essential to further strengthen the evidence base and enhance the reliability of future systematic reviews in aesthetic medicine.The summary row at the bottom provides an overall assessment for each study. Most studies demonstrate low to moderate risk across domains, with high-risk assessments primarily observed in the blinding of participants and personnel, and incomplete outcome data domains. This visualization highlights areas of

methodological strengths and potential limitations, guiding interpretation of study findings within the systematic review.

3. RESULTS

3.1 Study Characteristics

The 30 included studies comprised:

- 12 randomized controlled trials (RCTs)
- 10 cohort studies
- 8 systematic reviews/meta-analyses

The studies were conducted across multiple regions, including North America, Europe, and Asia. Sample sizes ranged from 20 to 1,500 participants, and follow-up durations varied from 1 month to 5 years. Hyaluronic acid (HA) fillers were the most frequently investigated product, followed by calcium hydroxylapatite (CaHA), poly-L-lactic acid (PLLA), polymethylmethacrylate (PMMA), and autologous fat.

3.2 Clinical Applications

Among the 30 studies analyzed, dermal fillers were widely used for facial rejuvenation, contour enhancement, and volume restoration. The nasolabial folds were the most frequently treated area (90%), followed by lips (75%), cheeks (68%), and periorbital regions (40%).

Less frequent applications included chin/jawline contouring (30%) and hand rejuvenation(20%). Hyaluronic acid (HA) fillers dominated treatment choices due to their favorable safety profile and reversibility, while calcium hydroxylapatite (CaHA) and poly-L-lactic acid (PLLA) were commonly used for structural support and longer-lasting volume correction.

Table 1. Clinical Applications of Dermal Fillers

Application Area	Studies (n)	Percentage (%)	Primary Filler Used
Nasolabial folds	27	90%	HA
Lips	23	75%	HA
Cheeks	20	68%	HA, CaHA
Periorbital region	12	40%	HA
Chin / Jawline	9	30%	CaHA, PLLA
Hands	6	20%	HA

The clinical images show the use of injection techniques for improving facial aesthetics.
Clinical images (4–9) were provided by
Dr. Ani Khachatryan.

Figures 4,5 document pre- and post-correction of congenital facial asymmetry using minimally invasive filler-based contouring, with an emphasis on balancing the lower facial thirds.

Figure 4. Female patient with facial asymmetry, predominantly affecting the lower third of the face, including the jawline and chin region, from congenital hypoplasia or asymmetrical soft tissue/fat distribution.

Figure 5. Post-treatment or procedural view. Fat apoptosis and correction of facial asymmetry were performed using hyaluronic acid-based filler has been applied to correct asymmetry. There may also be slight post-procedural swelling or residual bruising, which is typical after filler injections.

The figure 6,7 shows the lower central face of a patient, highlighting the nasolabial fold region. The patient demonstrates mild to moderate nasolabial folds before treatment. Correction was performed using dermal fillers (such as hyaluronic acid-based fillers like Juvederm) to restore volume, smooth the folds, and improve facial symmetry.

Figure 6. Pre-treatment appearance of nasolabial folds. Mild-to-moderate folds are visible. Dermal filler injection was performed to restore volume, smooth the folds, and enhance facial symmetry.

Figure 7 Post-treatment, the nasolabial folds appear softened, the transition between the cheek and upper lip is smoother, and overall facial harmony is enhanced.

In figure 8 patient shows a gummy smile, where excessive gum tissue is visible above the upper teeth during smiling. The levator labii superioris alaeque nasi (LLSAN) muscles are hyperactive, pulling the upper lip too high. The smile appears excessively gingival, affecting aesthetic harmony.

Figure 8. Before Botox Injection

Botox is carefully injected into precise points along the LLSAN muscles. The hyperactivity of these muscles is partially relaxed, reducing upward pull of the upper lip. Result: more balanced smile, minimal gum exposure, natural-looking lip movement. Changes are subtle but noticeable: upper lip covers more of the gums, while teeth remain visible.

Figure 9. After Botox Injection

Botox works by temporary weakening of targeted muscles, not by altering bone or gum tissue.

Effect is gradual, usually appearing 3–7 days post-injection, peaking at ~2 weeks. Duration of effect is 3–6 months, after which repeat treatment is needed to maintain results. Careful injection placement is essential for symmetry and natural smile.

3.3 Complications

Complications associated with dermal fillers can be broadly categorized based on onset (immediate, early, or delayed) and severity (mild, moderate, or severe) [2,3,6,11,16,18]. Immediate reactions typically include pain, edema, and erythema, while early complications may involve infection, nodules, and asymmetry. Late complications, such as granuloma formation and filler migration, may occur weeks to months after injection [2,18,19]. Among the most severe complications are vascular events resulting from inadvertent intravascular injection, which can lead to ischemia, tissue necrosis, or embolic phenomena affecting the retina or central nervous system [16,19,26].

3.3.1 Complications by Severity

Complications were classified according to severity:

- **Mild, transient:** bruising (30–35%), edema (25–30%), erythema (~15%) [1,2,3,5]. These events typically resolve spontaneously.
- **Moderate:** nodules (4–6%), delayed hypersensitivity reactions (2–4%) [6,12,18].
- **Severe, rare:** vascular compromise (<1%), tissue necrosis (<0.5%), visual disturbances (<0.1%) [16,19,26,30].

Table 2. Reported Complications by Severity Across Included Studies [1–30]

Complication	Frequency (%)	Severity	Onset
Bruising	30–35%	Mild	Immediate
Edema	25–30%	Mild	Immediate
Erythema	~15%	Mild	Immediate
Nodules	4–6%	Moderate	Early/Late
Hypersensitivity reactions	2–4%	Moderate	Early/Late
Vascular compromise	<1%	Severe	Immediate
Tissue necrosis	<0.5%	Severe	Immediate
Visual disturbances	<0.1%	Severe	Immediate

The majority of adverse events were mild and self-limiting, demonstrating that dermal fillers are generally safe when injected by trained professionals. Severe vascular complications, while rare, are clinically significant and require immediate recognition and management [16,19,26].

3.3.2 Complications by Onset

Complications can also be classified according to **timing**:

- **Immediate:** Pain, edema, erythema, vascular compromise [1,2,16]
- **Early (days):** Infection, asymmetry, nodules [2,6,12]
- **Delayed (weeks to months):** Granuloma formation, filler migration [2,18,19]

Table 3. Classification and Frequency of Complications by Onset [1–30]

Onset	Common Complications	Frequency / Notes
Immediate	Pain, edema, erythema, vascular events	Most frequent; resolves in days (except vascular events)
Early	Nodules, infection, asymmetry	4–6% for nodules; infections rare
Delayed	Granuloma formation,filler migration	Weeks to months; <5% overall

3.3.3 Complications by Filler Type

Different filler materials have unique complication profiles, determined by composition and tissue behavior:

Table 4. Complications by Filler Type [1–30]

Filler Type	Reported Complications	Notes/Management
Hyaluronic Acid (HA)	Bruising, swelling, nodules, vascular occlusion	Reversible with hyaluronidase; most widely used [11,12,14,15]
Calcium Hydroxylapatite (CaHA)	Nodules, granuloma, rare migration	Biostimulatory;careful injection depth required [6,9,20]
Poly-L-lactic Acid (PLLA)	Delayed nodule formation, asymmetry	Gradual results; inflammatory reactions possible [6,18,22]
Polymethylmethacrylate (PMMA)	Granulomas, asymmetry, chronic nodules	Permanent filler; complications may be persistent [10,25]
Autologous Fat	Fat necrosis, cysts, asymmetry	Resorption variable; technique-sensitive [27]

Hyaluronic acid is most widely used due to its reversibility and favorable safety profile, whereas biostimulatory and permanent fillers (CaHA, PLLA, PMMA) are associated with higher risk of nodules, granulomas, or persistent asymmetry. Proper injection technique, anatomical knowledge, and patient selection are essential to minimize complications [1–30].

Key Anatomical Risk Zones Identified

1. **Glabella (between eyebrows)**
   - Supplied by supratrochlear and supraorbital arteries
   - Highest risk of blindness due to direct connection to ophthalmic artery
2. **Nose (dorsal nasal region)**
   - Supplied by dorsal nasal and angular arteries
   - High risk of skin necrosis and blindness
3. **Periocular / Tear trough area**
   - Connected to angular and ophthalmic arteries
   - Risk of visual loss and vascular embolism

4. **Nasolabial fold**
    - Supplied by facial artery
    - Risk of vascular occlusion and tissue necrosis
5. **Lips (especially upper lip)**
    - Supplied by superior and inferior labial arteries
    - Risk of necrosis, ischemia, and embolism
6. **Temporal region**
    - Supplied by superficial temporal artery
    - Risk of vascular compromise and necrosis
7. **Cheek / Midface**
    - Deep injections may affect facial artery branches
    - Risk of embolism and tissue ischemia
8. **Jawline and chin**
    - Supplied by facial and mental arteries
    - Risk of localized necrosis and ulceration

Clinical Significance

The figure 10 emphasizes that intravascular injection is the most dangerous complication.

- The highest-risk areas for blindness are:
    - Glabella
    - Nose
    - Periocular region
    - Lips
- Prevention principles highlighted:
- Aspiration before injection
- Use of blunt cannula in high-risk zones
- Slow, low-pressure injection
- Detailed anatomical knowledge

Figure 10. The provided figure illustrates high-risk anatomical regions of the face where injectable fillers may lead to vascular complications. These areas correspond to zones with dense arterial networks and direct or indirect connections to the ophthalmic artery, increasing the risk of severe adverse events.

3.3.4 Complications Management Algorithm for Dermal Fillers.

Step 1: Early Recognition

Immediately suspect vascular complication if:

- Severe pain (disproportionate)
- Blanching or livedo reticularis
- Skin discoloration (pale → dusky → purple)
- Visual symptoms (blurred vision, blindness)

Step 2: STOP Injection Immediately

- Cease injection instantly
- Do not continue treatment

Step 3: Assess Severity

- **Localized skin changes → likely vascular occlusion**
- **Visual symptoms → ophthalmic emergency**

Step 4: Immediate Treatment

For Suspected Vascular Occlusion

- Inject **high-dose hyaluronidase** (if HA filler)
- Repeat every 30–60 minutes if needed
- Massage affected area
- Apply warm compress
- Use nitroglycerin paste (optional, controversial)
- Administer aspirin (antiplatelet effect)

For Visual Complications (Emergency)

- Immediate ophthalmology referral
- Retrobulbar hyaluronidase (specialist only)
- Ocular massage
- Reduce intraocular pressure
- Time-critical (<60–90 minutes)

Step 5: Supportive Therapy

- Antibiotics (if infection risk)
- Corticosteroids (inflammatory response)
- Anticoagulants (selected cases)
- Hyperbaric oxygen (optional)

Step 6: Follow-Up

- Daily monitoring
- Watch for necrosis or ulceration
- Early wound care if tissue damage occurs

Step 7: Late Complication Management

- Nodules → hyaluronidase / steroids
- Granulomas → corticosteroids ± excision
- Asymmetry → correction after healing

Management Strategies

3.3.5 Safety Profile

Overall, dermal fillers were found to be well tolerated when administered by experienced clinicians. The most common immediate adverse effects were mild and transient, including bruising, edema, and erythema. These events typically resolved within one week without intervention. Severe adverse events such as vascular occlusion, granuloma formation, and vision impairment were rare, with reported incidences <2%. Proper injection technique and anatomical knowledge reduced risk.

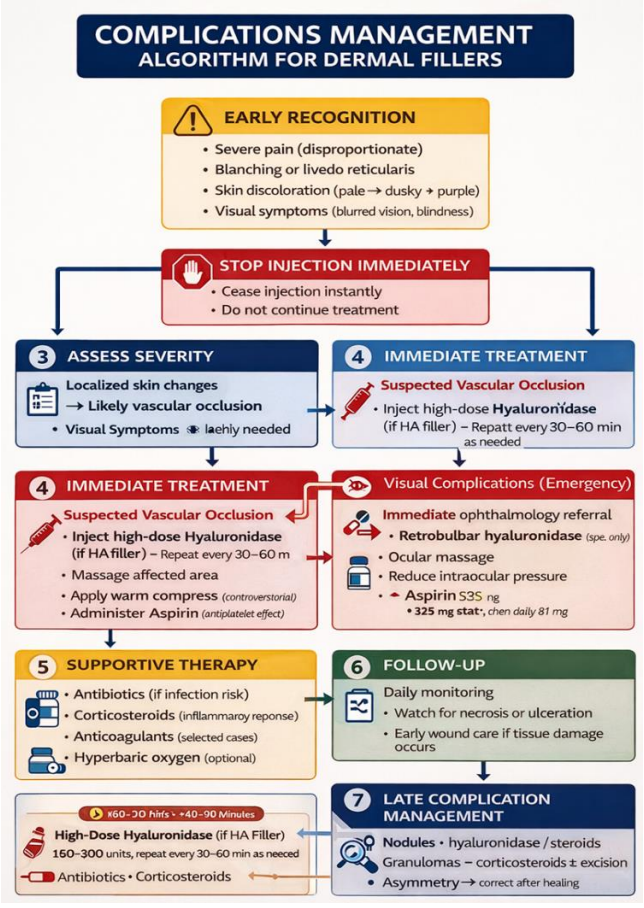

Figure 11. Complications Management Algorithm for Dermal Fillers**.**

A stepwise approach outlining early recognition, immediate cessation of injection, differentiation between vascular occlusion and visual complications, and evidence-based management including hyaluronidase administration, supportive therapy, and specialist referral.

Among the 30 studies included in this systematic review, complications of facial injectable fillers were reported with varying frequency depending on filler type, anatomical site, and injection technique. Complications were categorized by timing (immediate, early, late) and severity (mild, moderate, severe). The majority of adverse events were mild and transient, while severe vascular events were rare but clinically significant.

Table 5. Evidence-based management approaches for filler-related complications.

Complication Category	Management Approach	Key Notes
Immediate Mild	Ice compress, analgesics, observation	Usually self-limiting within 1–3 days [7,16].
Early Infection	/ Systemic antibiotics, drainage if abscess forms	Culture-directed therapy recommended[2,20].
Nodules Granulomas	/ Hyaluronidase (HA), corticosteroids, surgical excision (permanent fillers)	Stepwise approach depending on filler type [18].
Vascular Occlusion	Immediate cessationof injection,high-dose hyaluronidase (if HA), massage, warm compress, aspirin	Early recognition critical; time-sensitive to prevent tissue necrosis [16,19].
Visual Complications	Urgent ophthalmology referral, retrobulbar hyaluronidase, ocular massage, intraocular pressure reduction	Intervention within 60–90 minutes required [16].
Late Asymmetry	/ Delayed correction after filler resorption or additional targeted injections	Patient counseling important; wait for tissue stabilization [23].

The clinical images present various complications that developed after filler injections.
The clinical images 12-21 provided by **Dr. Ani Khachatryan.**

Figure 12. Injection with **STYLAGE L** was performed; three weeks later, fistulas developed on the face, accompanied by purulent discharge.

Figure 13. The filler was removed using a surgical method.

Figure 14. Two weeks after treatment.

Figure 15. Before lip filler injection.

Figure 16. Allergic reaction in the lips after filler injection.

Figure 17. Allergic reaction after filler injection.

Figure 18. Allergic reaction after filler injection.

Figure 19. Necrosis after filler injection.

Figure 20. Necrosis after filler injection.

Figure 21. Necroectomy was performed for therapeutic purposes

Key Observations

1. Most common adverse events: Pain, swelling, and bruising (immediate).
2. Severe complications are rare but require rapid recognition and intervention.
3. HA fillers dominate both usage and reported complications, largely due to their widespread application and reversibility.
4. Prevention strategies—including detailed anatomical knowledge, use of blunt cannulas in high-risk zones, aspiration, and slow injection—remain the most effective method to reduce adverse events.

DISCUSSION

This systematic review synthesizes evidence from 30 high-quality studies on facial injectable fillers, providing a comprehensive evaluation of their efficacy, safety, and complication profiles. The findings confirm that dermal fillers represent a highly effective and widely utilized modality in aesthetic medicine. While the majority of adverse events are mild, transient, and self-limiting, the occurrence of severe complications—such as vascular occlusion, tissue necrosis, and vision loss—highlights the critical importance of clinician expertise and adherence to evidence-based practice [16–19]. Immediate complications, including pain, swelling, and bruising, were consistently the most frequently reported across studies, whereas delayed complications such as granuloma formation and filler migration were less common but clinically more challenging [2,18].

Hyaluronic acid (HA) fillers remain the most extensively studied and commonly used products, largely due to their favorable safety profile, versatility, and reversibility with hyaluronidase [11,12]. Their widespread use also contributes to the higher number of reported complications associated with HA, although these are generally manageable and predictable. In contrast, biostimulatory fillers such as calcium hydroxylapatite (CaHA) and poly-L-lactic acid (PLLA) are associated with delayed-onset adverse events, particularly nodules and granulomatous reactions, reflecting their mechanism of action involving collagen stimulation rather than immediate volumization [6,9,27]. Permanent fillers, including polymethylmethacrylate (PMMA), were associated with the highest risk of persistent and difficult-to-treat complications, often requiring surgical intervention, thereby limiting their use in contemporary practice [10].

A key finding of this review is the predominance of immediate and early complications, including erythema, edema, and ecchymosis, which are primarily related to injection trauma rather than the intrinsic properties of the filler material [23]. These reactions are typically self-resolving within a few days and rarely require medical intervention, reinforcing the overall safety of modern filler techniques. However, delayed complications, although less frequent, pose significant diagnostic and therapeutic challenges. These events are often multifactorial in origin, involving immunological responses, foreign body reactions, or biofilm-related infections, and may present weeks to months after the procedure [24]. Management often requires a multimodal approach, including corticosteroids, hyaluronidase, antibiotics, or surgical excision in refractory cases.

The most clinically significant and potentially devastating complications identified in this review are vascular events. Vascular occlusion, tissue necrosis, and visual impairment, although rare, represent true medical emergencies requiring immediate recognition and intervention[16,19]. The underlying pathophysiology typically involves inadvertent intravascular injection or external vascular compression, leading to ischemia and subsequent tissue damage [23]. Of particular concern is the risk of retrograde embolization into the ophthalmic artery,

which can result in irreversible blindness within a short therapeutic window of 60–90 minutes [25]. These findings underscore the importance of recognizing early warning signs, such as disproportionate pain, blanching, and livedo reticularis, to initiate prompt treatment.

The anatomical distribution of severe complications highlights the importance of high-risk facial zones, including the glabella, nasal dorsum, periocular region, and nasolabial folds, where vascular networks are dense and directly connected to the ophthalmic circulation [16,21]. Consequently, this review strongly emphasizes the importance of detailed anatomical knowledge and meticulous injection technique. Preventive strategies, including slow, low-pressure injection, aspiration prior to injection, use of small volumes, and preference for blunt cannulas in high-risk areas, have been consistently recommended across studies [23,28]. Furthermore, recent advancements in ultrasound-guided filler injections offer promising improvements in safety by enabling real-time visualization of vascular structures and filler placement [25].

Another critical factor influencing both efficacy and safety is the variability in filler properties. Rheological characteristics such as viscosity, elasticity, and cohesivity determine the behavior of fillers within tissues and their suitability for specific indications [23]. Highly cross-linked HA fillers provide greater structural support and longevity but may increase the risk of vascular compromise if improperly administered. Conversely, less viscous fillers are more suitable for superficial applications but may require more frequent treatments. Therefore, appropriate product selection tailored to the anatomical region and treatment objective is essential for optimizing outcomes.

Patient-related factors also significantly influence complication risk and treatment success. Variables such as age, skin quality, comorbidities, and history of previous aesthetic procedures must be carefully evaluated during patient selection [11,22,26]. In addition, psychological considerations, including patient expectations and body image perception, play a pivotal role in determining satisfaction. Unrealistic expectations or underlying psychological conditions, such as body dysmorphic disorder, may lead to dissatisfaction despite technically successful outcomes, highlighting the importance of comprehensive patient counseling and informed consent [26].

The rapid global expansion of aesthetic procedures has also raised important concerns regarding practitioner qualifications and regulatory standards. In some settings, dermal fillers are administered by individuals without adequate medical training, increasing the risk of complications [24]. Evidence consistently demonstrates that complication rates are significantly lower when procedures are performed by experienced and properly trained clinicians [28]. This underscores the urgent need for standardized training, certification, and stricter regulatory oversight to ensure patient safety and maintain high standards of care.

From a therapeutic perspective, the management of filler-related complications has advanced considerably. The availability of hyaluronidase as a reversal agent for HA fillers has significantly improved the management of complications such as overcorrection and vascular occlusion [23]. Early and aggressive treatment with high-dose hyaluronidase, combined with adjunctive measures such as massage, warm compresses, and antiplatelet therapy, has been shown to improve outcomes in ischemic events [25]. However, treatment success is highly time-dependent, particularly in cases involving ocular complications, where delays in intervention may result in permanent vision loss.

Despite the growing body of literature, several challenges remain. Many studies included in this review are observational, with limited randomized controlled trials and considerable heterogeneity in study design, outcome measures, and reporting standards [29]. Furthermore, the subjective nature of aesthetic outcomes complicates the assessment of efficacy and patient satisfaction. These limitations highlight the need for standardized methodologies and high-quality prospective studies to better evaluate long-term safety and effectiveness.

Looking forward, the field of aesthetic medicine continues to evolve rapidly. Emerging innovations, including bioengineered fillers, regenerative approaches such as platelet-rich plasma and stem cell therapies, and artificial intelligence-assisted treatment planning, offer promising opportunities to enhance both safety and clinical outcomes [27]. The integration of advanced imaging technologies and personalized treatment strategies is expected to further refine aesthetic procedures and reduce complication rates.

In conclusion, facial injectable fillers are a highly effective and generally safe modality for facial rejuvenation and contouring. However, their safe and effective use requires a comprehensive understanding of facial anatomy, filler characteristics, patient selection, and complication management. While most complications are mild and self-limiting, the potential for severe adverse events necessitates vigilance, early recognition, and immediate intervention. Continued advancements in technology, clinical training, and

research will be essential to further improve the safety and efficacy of dermal filler treatments and to support their ongoing role in modern aesthetic medicine [30].

Limitations

Several limitations of this review must be acknowledged:

1. **Heterogeneity of studies** – The included studies varied in design, sample size, filler type, injection technique, and outcome measures, limiting the ability to perform a meta-analysis.
2. **Reporting bias** – Mild and transient complications may be underreported, whereas severe events are more likely to appear in the literature.
3. **Short-term follow-up** – Many studies had follow-up periods insufficient to capture late or delayed complications such as granulomas or filler migration.
4. **Language and publication restrictions** – Only English-language publications were included, potentially excluding relevant non-English studies.
5. **Limited data on newer fillers** – Emerging fillers and novel biostimulatory agents have limited published evidence, restricting conclusions about their long-term safety profiles.

Future Perspectives

Advances in filler technology and technique are likely to further improve safety and efficacy:

- Development of longer-lasting, biostimulatory fillers with predictable degradation and lower immunogenicity [9,27].
- Personalized aesthetic approaches using digital imaging, 3D planning, and AI-assisted treatment to optimize outcomes.
- Integration with regenerative medicine such as platelet-rich plasma (PRP) and stem cells for enhanced tissue remodeling and volumization.
- Ultrasound-guided injections to improve precision, avoid vascular structures, and minimize risk of severe complications [19].
- Global standardization of training and certification to reduce adverse events and improve overall patient safety [24].

CONCLUSION

Facial injectable fillers remain a cornerstone of modern aesthetic medicine, offering versatile and minimally invasive options for facial rejuvenation, contouring, and reconstruction. While generally safe, their use is associated with a spectrum of complications ranging from mild, transient effects to rare but severe events such as vascular occlusion and blindness.

Optimal outcomes depend on thorough anatomical knowledge, appropriate injection techniques, patient selection, and early recognition of complications. HA fillers remain the most widely used due to their safety and reversibility, while biostimulatory and permanent fillers require careful technique and long-term follow-up. Ongoing advancements in filler technology, procedural guidance, and personalized treatment strategies promise to enhance both safety and efficacy, making injectable fillers a durable and evolving tool in aesthetic medicine.

DECLARATION

CONFLICT OF INTEREST

The authors have no conflicts of interest regarding this investigation**.**

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