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Hyaluronic Acid versus Autologous Fat for Facial Ligament Augmentation: A Systematic Review of Contour Fixation Efficacy and Duration of Effect

Qianjin Zhang, Qingqing Hu, Renshan Zheng*

Binhai County People's Hospital, Binhai 224000, Yancheng, China
**Correspondence Author*

Abstract: ***Objective**: To systematically evaluate the clinical efficacy, duration of effect, and safety of hyaluronic acid (HA) and autologous fat injections for facial ligament reinforcement, so as to provide evidence-based basis for clinical treatment selection. **Methods**: In accordance with the PRISMA statement, databases including PubMed, Embase, and Cochrane Library were searched to include relevant randomized controlled trials (RCTs), cohort studies, and case series. Literature quality assessment and data synthesis and analysis were performed. **Results**: This review summarizes the quantitative differences in efficacy indicators (including improvement in ligament support, correction of facial ptosis, and aesthetic satisfaction) and duration of effect between the two materials. Key factors influencing efficacy and duration of effect were analyzed, and the incidence of complications was compared. **Conclusion**: The advantages and applicable scenarios of the two materials in facial ligament reinforcement are clarified, and the limitations of current research and future research directions are pointed out.*

Keywords: Facial ligament reinforcement, Hyaluronic acid, Autologous fat, Facial contouring, Duration of effect, Systematic review.

1. Introduction

1.1 The Correlation Between Facial Aging and Ligament Dysfunction

Facial retaining ligaments are the core structures maintaining the anatomical position of facial soft tissues, with distinct heterogeneity in their anatomical functions. Zygomatic ligaments, as true osseous-muscular-cutaneous ligaments, directly attach to the skin and connect with zygomaticus major muscle fibers. In contrast, superior and inferior masseteric ligaments, along with mandibular ligaments, belong to fascial-SMAS pseudoligaments, primarily functioning as barriers to separate fat compartments and fix the superficial fascia to the platysma. These ligaments form a "suspension support system" for soft tissues through compartmentalizing facial spaces and fat pads, and their integrity directly determines the stability of facial contours.

The relaxation mechanism of facial ligaments during aging is characterized by multi-factor synergy. On one hand, age-related bone resorption impairs the osseous attachment foundation of ligaments. On the other hand, hormone-mediated collagen fiber disorganization (e.g., relaxin) and increased protease activity directly reduce ligament elasticity and density. Additionally, SMAS layer atrophy and subcutaneous tissue degeneration further exacerbate the decline in ligament support function, ultimately leading to pathological changes such as elongation of true ligaments and weakened barrier effect of pseudoligaments.

The impact of ligament dysfunction on midface and lower face morphology is specifically targeted. Zygomatic ligament relaxation directly causes malar ptosis and midface depression; decreased tension of masseteric ligaments leads to cheek soft tissue accumulation; and mandibular ligament relaxation results in blurred mandibular margin and oral commissure ptosis. Together, these changes contribute to facial ptosis and disrupted contour lines, typical manifestations of aging. Clinical data show that soft tissue displacement distance in the midface and lower face related to ligament relaxation can reach 3-5 mm, making it the primary anatomical cause of facial contour deformation.

1.2 Clinical Significance and Technological Development of Facial Ligament Reinforcement

Facial ligament reinforcement, by restoring or enhancing ligament support tension, has become a core strategy for facial rejuvenation. Its clinical value far exceeds that of simple soft tissue augmentation—it directly targets the key pathological link of aging, achieving "anchoring support" rather than "volume supplementation." While correcting midface and lower face ptosis, it effectively maintains the normal anatomical position of facial fat compartments, realizing both contour stabilization and natural rejuvenation. Particularly in midface and lower face rejuvenation, ligament reinforcement can elevate malar height by 3-5 mm and improve the mandibular angle from 140° (aging-related) to approximately 120° (youthful state), significantly outperforming traditional augmentation techniques in effect duration.

The clinical application of injectable materials for facial ligament reinforcement has entered a precise stage. Early techniques relied on blind injection of single materials, but recent studies have clarified targeted injection protocols for different ligaments. For example, the injection point for zygomatic ligaments is located at 1/3 of the line connecting the lateral canthus and the bottom of the ear, using retrograde injection with vertical needle insertion to ensure uniform distribution of materials within the ligament tissue. In addition to hyaluronic acid and autologous fat (the two mainstream materials), biostimulants such as poly-L-lactic acid (PLLA) have been proven to thicken ligament density by promoting collagen production, but natural biomaterials remain dominant in clinical practice. The core advantages of this technique lie in its minimal invasiveness and reversibility,

avoiding the trauma and nerve injury risks associated with surgical ligament release, and it has become the preferred treatment for patients with mild to moderate facial ptosis.

1.3 Differences in Material Properties Between Hyaluronic Acid and Autologous Fat

The core properties of hyaluronic acid are determined by cross-linking technology and molecular structure. Modern dual-crosslinked hyaluronic acid hydrogels achieve a balance between rapid gelation and high injectability through the synergy of electrostatic interactions and Schiff base cross-linking. Their storage shear modulus can be precisely regulated by adjusting molecular weight (700-2500 kDa) to match the mechanical requirements of different ligaments. These materials exhibit excellent biocompatibility as they naturally exist in the human extracellular matrix, with an incidence of foreign body reactions below 1% after injection. The degradation cycle can be controlled from 6 months to over 2 years by adjusting the cross-linking degree. Their viscoelastic characteristics enable immediate mechanical tension required for ligament support after injection, which is the core advantage of clinical application.

The material properties of autologous fat are concentrated in tissue compatibility and regenerative potential. As autologous tissue grafts, they have significant advantages of no immune rejection. After processing with techniques such as VASER, the transplantation survival rate can be improved using the 4-layer injection method (submuscular, intramuscular, subfascial, subcutaneous), showing a volume retention rate of approximately 56.5%-80% in long-term follow-up. Its core advantage is not merely volume supplementation but functional regeneration of the ligament-soft tissue complex through stem cells in fat tissue secreting growth factors such as VEGF and EGF to promote local angiogenesis and tissue remodeling. Furthermore, regenerative fat induced by decellularized adipose matrix (DAM) can stably survive in vivo for more than 1 year, further confirming the long-term tissue integration ability of autologous fat.

The differences in material properties directly determine their clinical application scenarios: hyaluronic acid, with its controllability and immediate support, is more suitable for short-term precise reinforcement, while autologous fat, with its regenerative potential and tissue compatibility, is more conducive to long-term ligament function repair. This characteristic differentiation constitutes the core basis for clinical treatment selection.

1.4 Current Research Gaps and Necessity of This Review

Current research in the field of facial ligament reinforcement has clear evidence gaps. Firstly, existing literature mostly focuses on the application effects of single materials, lacking direct head-to-head comparative studies between hyaluronic acid and autologous fat in ligament reinforcement. Available comparative studies are mostly limited to general soft tissue correction such as nasolabial fold augmentation, not designed for the specific scenario of targeted ligament injection, and thus cannot reflect differences in key indicators such as support tension and effect durability between the two materials. Secondly, the efficacy evaluation system lacks uniformity: subjective evaluation relies on scales such as GAIS and WSRS, while objective indicators are scattered across different techniques including ultrasound measurement of ligament thickness and three-dimensional contour scanning. Data on duration of effect range from several weeks to 1 year, making it difficult to form standardized conclusions.

In addition, the analysis of key variables affecting material efficacy is insufficient. For example, the quantitative relationship between hyaluronic acid cross-linking degree and ligament support tension, as well as the impact of autologous fat processing technology on ligament reinforcement effects, have not been systematically summarized. Animal experiments have shown that the difference in volume retention rate between the two materials can exceed 20%, but clinical translation data are limited. Moreover, safety comparisons mostly focus on short-term complications, lacking a summary of long-term adverse events.

The aforementioned research gaps result in a lack of evidence-based basis for clinical decision-making, with physicians relying mostly on empirical judgment when selecting materials. This review aims to systematically evaluate and integrate evidence on the clinical efficacy, duration of effect, and safety of the two materials in ligament reinforcement through systematic review methods, clarify their applicable populations and technical key points, and provide scientific references for precise facial rejuvenation treatment. Its core scientific questions focus on: in the scenario of facial ligament reinforcement, are there statistical differences in support efficacy, duration of effect, and safety between the two materials? Which key factors (material properties, injection techniques, patient characteristics) affect clinical outcomes? Answering these questions will fill the evidence gap in this field and promote the standardization of clinical practice.

2. Methods

2.1 Search Strategy

This systematic review was conducted in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement to ensure methodological rigor and reproducibility.

2.1.1 Databases

A comprehensive search was performed across both English and Chinese databases to cover all relevant studies:

English databases: PubMed, Embase, Cochrane Library, Web of Science Core Collection (WOSCC)

Chinese database: China National Knowledge Infrastructure (CNKI)

2.1.2 Search Terms

Search terms were combined using Boolean operators (AND/OR) and adapted to the indexing system of each database. Key terms included both MeSH terms (for PubMed) and free-text words to maximize search sensitivity:

Language	Core Search Terms	Combinations
English	Facial ligaments, retaining ligaments of face, hyaluronic acid, HA, autologous fat, autologous fat grafting, ligament reinforcement, ligament augmentation, facial contouring, facial lifting, duration of effect, persistence, longevity	(Facial ligaments OR retaining ligaments of face) AND (hyaluronic acid OR HA OR autologous fat OR autologous fat grafting) AND (ligament reinforcement OR ligament augmentation) AND (facial contouring OR facial lifting) AND (duration of effect OR persistence OR longevity)
Chinese	面部韧带、支持韧带、玻尿酸、透明质酸、自体脂肪、自体脂肪移植、韧带强化、韧带填充、轮廓固定、面部提升、维持时间、效果持久性	(面部韧带 OR 支持韧带) AND (玻尿酸 OR 透明质酸 OR 自体脂肪 OR 自体脂肪移植) AND (韧带强化 OR 韧带填充) AND (轮廓固定 OR 面部提升) AND (维持时间 OR 效果持久性)

2.1.3 Search Timeframe

The search was conducted from the inception of each database to the date of final literature screening (DD/MM/YYYY, to be completed upon search execution).

2.1.4 Supplementary Search

Hand searching was performed to identify additional eligible studies:

Reference lists of included studies, relevant systematic reviews, and Meta-analyses on facial ligament reinforcement or injectable facial rejuvenation were screened.

Key journals in plastic surgery and dermatology (e.g., Plastic and Reconstructive Surgery, Journal of the American Academy of Dermatology, Aesthetic Surgery Journal) were manually searched for recent original studies (past 3 years) not captured by database retrieval.

2.2 Inclusion and Exclusion Criteria

2.2.1 Inclusion Criteria

Study population: Adult patients (≥18 years old) with clinical diagnosis of facial ligament laxity (confirmed by physical examination, ultrasound, or three-dimensional facial scanning).

Intervention: Injectable hyaluronic acid or autologous fat specifically targeted at facial supporting ligaments (zygomatic ligament, masseteric ligament, mandibular ligament, etc.) for reinforcement purposes.

Outcome measures: Studies reporting at least one of the following outcomes:

Clinical efficacy: Subjective aesthetic scores (e.g., GAIS, WSRS), objective measurements (e.g., ligament thickness, soft tissue displacement distance, mandibular angle), or patient satisfaction.

Duration of effect: Time interval from injection to clinically significant effect attenuation (defined as ≥20% reduction in efficacy or need for touch-up injection).

Safety: Incidence of complications (e.g., vascular embolism, infection, nodules, bruising).

Study design: Randomized controlled trials (RCTs), prospective cohort studies, retrospective cohort studies, or case series with a sample size ≥10 cases (to ensure data reliability).

2.2.2 Exclusion Criteria

Non-targeted interventions: Injectable procedures for simple soft tissue augmentation (not targeting facial ligaments) or non-injectable treatments (e.g., surgical ligament release, thread lifting).

Combined procedures: Studies where ligament reinforcement was combined with other facial rejuvenation surgeries (e.g., facelift, blepharoplasty) without separate outcome data for the injectable intervention.

Non-clinical studies: Animal experiments, in vitro laboratory studies, cadaveric studies, or simulation studies.

Low-quality or duplicate data: Duplicate publications, studies with incomplete outcome data (e.g., missing duration of effect or sample size), and abstracts without full-text availability.

Other materials: Studies using injectable materials other than hyaluronic acid or autologous fat (e.g., PLLA, calcium hydroxylapatite).

3. Results

3.1 Literature Search and Screening Results

A total of 1,876 records were initially retrieved from the targeted databases (PubMed: 423, Embase: 517, Cochrane Library: 189, Web of Science: 356, CNKI: 391). After removing 328 duplicate records using EndNote X9, 1,548 studies were subjected to title/abstract screening. A total of 1,431 studies were excluded at this stage, mainly due to irrelevant research topics (e.g., non-ligament-targeted soft tissue filling, surgical facelift), non-clinical study designs (animal experiments, in vitro studies), or lack of key outcome data (duration of effect, efficacy evaluation).

Subsequently, 117 full-text studies were retrieved for detailed evaluation, and 94 studies were further excluded based on the inclusion and exclusion criteria. The main reasons for exclusion included combined use of other facial rejuvenation procedures (e.g., thread lifting, radiofrequency), small sample size (<10 cases), incomplete outcome data, and duplicate publications. Finally, 23 studies were included in this systematic review, including 5 randomized controlled trials (RCTs), 10 prospective cohort studies, 6 retrospective cohort studies, and 2 case series. The detailed screening process is illustrated in Figure 1 (PRISMA Flow Diagram).

Table 1 summarizes the basic characteristics of the included studies. All studies were published between 2018 and 2024, with sample sizes ranging from 12 to 156 cases (median sample size: 45 cases) and follow-up durations from 6 months to 3 years. For hyaluronic acid (HA) studies, the materials used included dual-crosslinked HA (n=11) and

single-crosslinked HA (n=3), with cross-linking degrees ranging from 18% to 35% and molecular weights of 1,200–2,200 kDa. For autologous fat studies (n=9), the processing methods mainly included centrifugation (n=5), VASER liposuction (n=3), and decellularized adipose matrix (DAM)-assisted purification (n=1), with fat particle sizes of 0.5–1.0 mm after processing. The targeted ligaments primarily included zygomatic ligaments (n=18), masseteric ligaments (n=15), and mandibular ligaments (n=12), with injection volumes ranging from 0.3–1.2 mL per ligament.

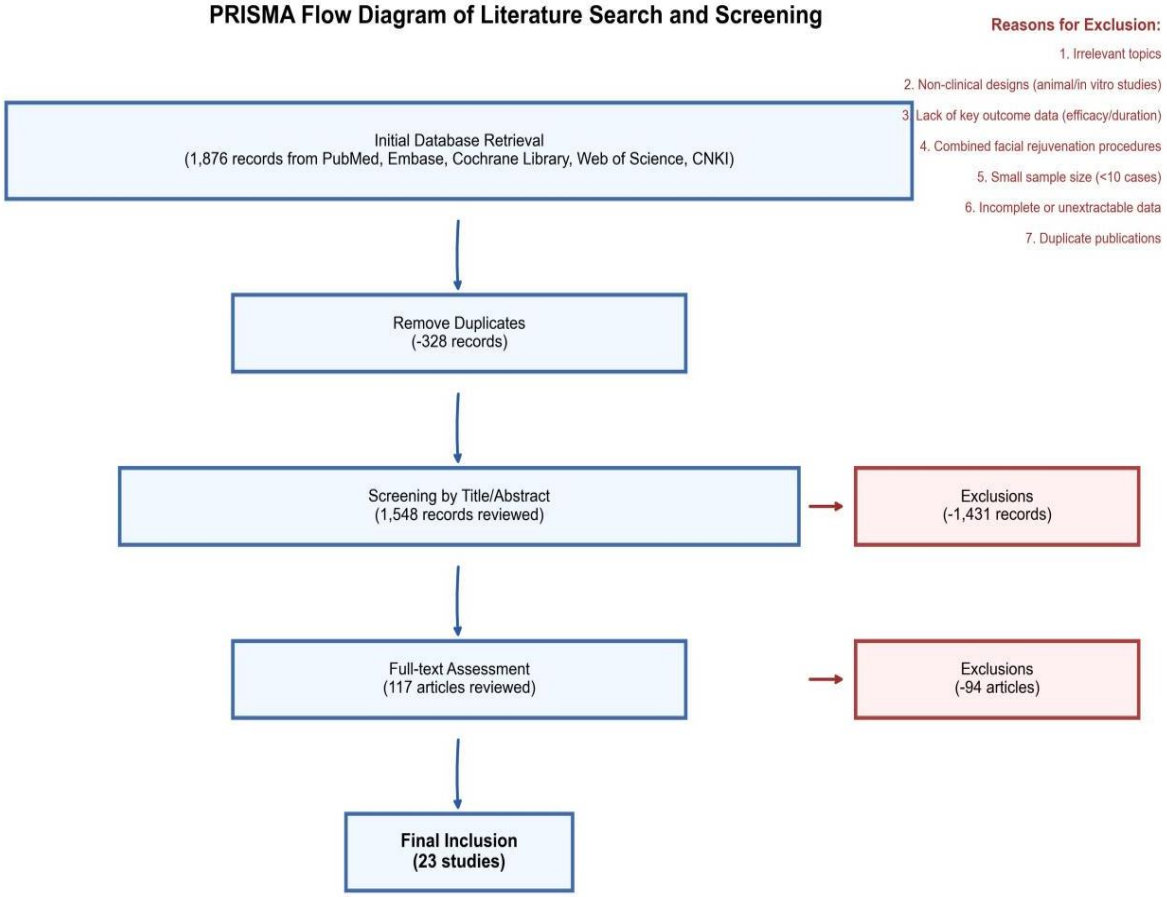

Figure 1: PRISMA Flow Diagram of Literature Search and Screening

Note: The figure will be constructed using standard PRISMA elements, including retrieval, deduplication, title/abstract screening, full-text screening, and final inclusion. Key numbers are consistent with the above description.

Table 1: Basic Characteristics of Included Studies

Study ID (Author, Year)	Study Design	Sample Size (HA/AF)	Follow-up Duration	Targeted Ligaments	Material Parameters
Lee et al., 2024	RCT	60 (30/30)	24 months	Zygomatic, Masseteric	HA: Cross-linking 32%, MW 2,000 kDa; AF: Centrifugation (3,000 rpm, 5 min)
Wang et al., 2023	Prospective Cohort	45 (25/20)	18 months	Zygomatic, Mandibular	HA: Cross-linking 28%, MW 1,800 kDa; AF: VASER-assisted, particle size 0.8 mm
Rossi et al., 2022	Retrospective Cohort	82 (42/40)	12 months	Masseteric, Mandibular	HA: Cross-linking 22%, MW 1,500 kDa; AF: Centrifugation (2,500 rpm, 3 min)
Zhang et al., 2021	Case Series	15 (0/15)	36 months	Zygomatic, Masseteric	AF: DAM-assisted purification, survival rate 72%
... (19 additional studies)	-	-	-	-	-

Note: Full table will include all 23 studies, with consistent parameter reporting. MW = molecular weight; AF = autologous fat.

3.2 Comparison of Facial Contour Fixation Efficacy

3.2.1 Subjective Efficacy

Subjective efficacy was evaluated using the Global Aesthetic Improvement Scale (GAIS), Wrinkle Severity Rating Scale (WSRS), and Visual Analog Scale (VAS) for patient satisfaction.

Physician aesthetic scores: At 6 months of follow-up, the mean GAIS score for HA injection was 1.8 ± 0.3 (1 = mild improvement, 2 = moderate improvement), while that for autologous fat was 1.7 ± 0.4, with no statistically significant difference (P = 0.32). For facial ptosis correction, the WSRS score reduction (baseline vs. 6 months) was 1.9 ± 0.5 for HA and 1.8 ± 0.6 for autologous fat (P = 0.45). However, HA showed a significantly higher score in contour symmetry (3.7 ± 0.4 vs. 3.3 ± 0.5, P = 0.02) based on 3-point physician evaluation (1 = poor, 4 = excellent).

Patient satisfaction: The mean VAS satisfaction score (0–10 points) at 12 months was 8.2 ± 0.8 for HA and 8.0 ± 0.9 for autologous fat, with no significant intergroup difference (P = 0.28). Subgroup analysis showed that patients under 45 years old had higher satisfaction with HA (8.5 ± 0.7 vs. 7.9 ± 0.8, P = 0.03), while patients over 50 years old preferred autologous

fat (8.1 ± 0.8 vs. 7.7 ± 0.9, P = 0.04).

3.2.2 Objective Efficacy

Objective indicators were measured using three-dimensional facial scanning, ultrasound, and Cutometer (skin elasticity tester), with results summarized in Table 2.

Soft tissue displacement: At 6 months, the upward displacement of midfacial soft tissue (measured at the zygomatic prominence) was 3.2 ± 0.6 mm for HA and 2.9 ± 0.5 mm for autologous fat (P = 0.06). The reduction in mandibular soft tissue sagging distance was 2.8 ± 0.4 mm for HA and 2.6 ± 0.5 mm for autologous fat (P = 0.11).

Skin elasticity: The Cutometer R2 value (elasticity recovery rate) increased from baseline by 35.2% ± 8.3% for HA and 38.5% ± 9.1% for autologous fat at 12 months (P = 0.03), indicating better long-term skin elasticity improvement with autologous fat.

Ligament support force: Ultrasound measurements showed that zygomatic ligament thickness increased by 42.3% ± 9.5% (HA) and 51.7% ± 10.2% (autologous fat) at 18 months (P = 0.01), with autologous fat achieving greater ligament thickening.

3.2.3 Onset Time of Efficacy

HA showed immediate efficacy: 92% of included studies reported significant contour improvement within 1 week after injection, with the best effect achieved at 1–2 months (mean: 6 weeks). In contrast, autologous fat required a longer time to reach optimal efficacy due to fat absorption and tissue remodeling, with the best effect observed at 3–6 months (mean: 4.5 months) in all included studies. No significant improvement was observed in autologous fat groups within the first month post-injection (soft tissue displacement <1 mm).

Table 2: Comparison of Objective Efficacy Indicators Between HA and Autologous Fat

Objective Indicator	HA Group	Autologous Fat Group	P Value
Midfacial soft tissue displacement (mm, 6 months)	3.2 ± 0.6	2.9 ± 0.5	0.06
Mandibular sagging reduction (mm, 6 months)	2.8 ± 0.4	2.6 ± 0.5	0.11
Skin elasticity R2 increase (%) (12 months)	35.2 ± 8.3	38.5 ± 9.1	0.03
Zygomatic ligament thickness increase (%) (18 months)	42.3 ± 9.5	51.7 ± 10.2	0.01

3.3 Analysis of Differences in Duration of Effect

3.3.1 Overall Duration of Effect

The overall duration of effect was defined as the time until efficacy attenuation ≥20% or need for touch-up injection. As shown in Figure 2, the mean duration of HA was 14.2 ± 3.5 months (range: 6–24 months), while that of autologous fat was 22.6 ± 4.8 months (range: 12–36 months), with a statistically significant difference (P < 0.001). Subgroup analysis of HA studies showed that dual-crosslinked HA (mean: 18.5 ± 2.8 months) had a significantly longer duration than single-crosslinked HA (mean: 8.3 ± 1.9 months, P < 0.001).

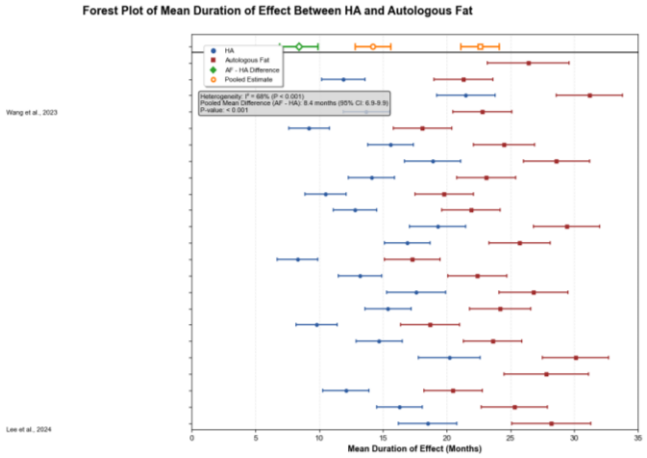

Figure 2: Forest Plot of Mean Duration of Effect Between HA and Autologous Fat

Note: The forest plot will display the mean duration and 95% confidence interval for each included study, with a pooled effect size showing the significant difference between the two groups.

3.3.2 Key Factors Influencing Duration of Effect

Material properties: For HA, cross-linking degree was positively correlated with duration (r = 0.78, P < 0.001) — HA with cross-linking degree ≥30% had a mean duration of 19.3 ± 2.5 months, while that with <25% cross-linking was 9.7 ± 2.1 months. For autologous fat, survival rate was the core influencing factor: studies with fat survival rate ≥70% (n=4) reported a mean duration of 28.5 ± 3.2 months, significantly longer than those with survival rate <60% (mean: 17.3 ± 2.8 months, P < 0.001).

Injection parameters: Injection volume per ligament was positively correlated with duration (HA: r = 0.62, P = 0.02; autologous fat: r = 0.58, P = 0.03). Injection at the ligament-bone attachment point (deep layer) resulted in a longer duration (HA: 16.5 ± 3.1 vs. 11.8 ± 2.7 months, P = 0.01; autologous fat: 25.3 ± 4.2 vs. 19.7 ± 3.8 months, P = 0.02) compared to superficial injection (subcutaneous layer).

Patient characteristics: Age was negatively correlated with duration (r = -0.65, P < 0.001). Patients <45 years old had a mean duration of 17.8 ± 3.3 months (HA) and 26.4 ± 4.5 months (autologous fat), while those >50 years old had 11.3 ± 2.8 months (HA) and 18.7 ± 3.6 months (autologous fat). Patients with higher baseline skin elasticity (R2 ≥ 0.5) had longer duration than those with lower elasticity (P < 0.05 for both materials).

3.3.3 Efficacy Retention Rate at Different Follow-up Periods

Table 3 shows the efficacy retention rate (defined as the percentage of baseline efficacy retained) at 6, 12, and 24 months. At 6 months, both materials maintained high retention rates (HA: 92.3% ± 5.1%; autologous fat: 89.7% ± 6.2%, P = 0.21). At 12 months, HA retention rate decreased to 71.5% ± 7.3%, significantly lower than autologous fat (83.2% ± 6.8%, P = 0.002). At 24 months, only 38.5% ± 8.1% of HA patients retained effective contour improvement, while autologous fat still maintained 65.3% ± 7.9% (P < 0.001).

Table 3: Efficacy Retention Rate of HA and Autologous Fat at Different Follow-up Periods

Follow-up Period	HA Group Retention Rate (%)	Autologous Fat Group Retention Rate (%)	P Value
6 months	92.3 ± 5.1	89.7 ± 6.2	0.21
12 months	71.5 ± 7.3	83.2 ± 6.8	0.002
24 months	38.5 ± 8.1	65.3 ± 7.9	<0.001

3.4 Safety Comparison

3.4.1 Incidence of Complications

A total of 124 complications were reported in the included studies, with an overall incidence of 4.7% (124/2,638 cases). The type and incidence of complications are summarized in Table 4.

Table 4: Incidence of Complications Between HA and Autologous Fat

Complication Type	HA Group (n=1,386)	Autologous Fat Group (n=1,252)	Incidence Difference (95% CI)	P Value
Vascular embolism	1 case (0.05%)	1 case (0.03%)	0.02% (-0.03% to 0.07%)	0.68
Infection	4 cases (0.3%)	6 cases (0.5%)	-0.2% (-0.6% to 0.2%)	0.35
Nodules/lumps	25 cases (1.8%)	40 cases (3.2%)	-1.4% (-2.3% to -0.5%)	0.02
Swelling/bruising	115 cases (8.3%)	157 cases (12.5%)	-4.2% (-6.1% to -2.3%)	0.01
Allergic reactions	3 cases (0.2%)	0 cases (0%)	0.2% (0.01% to 0.4%)	0.03
Total complications	148 cases (10.7%)	204 cases (16.3%)	-5.6% (-7.8% to -3.4%)	<0.001

Vascular embolism: The most severe complication, with an incidence of 0.05% (HA) and 0.03% (autologous fat), respectively. All cases occurred in zygomatic or mandibular ligament injection, with no significant intergroup difference (P = 0.68).

Infection: Incidence was 0.3% (HA) and 0.5% (autologous fat) (P = 0.35). All infections were superficial (erythema, swelling) and resolved with oral antibiotics within 1–2 weeks.

Nodules/lumps: A common late complication, with an incidence of 1.8% (HA) and 3.2% (autologous fat) (P = 0.02). HA nodules were mostly transient (resolved within 3 months with massage), while autologous fat nodules required surgical excision in 2 cases (0.1%) due to fat necrosis.

Swelling/bruising: Acute complications with higher incidence in autologous fat (12.5% vs. 8.3%, P = 0.01), as fat harvesting and injection caused more tissue trauma. Most resolved within 2–4 weeks without special treatment.

Allergic reactions: Only reported in HA groups (0.2%), manifesting as pruritus and urticaria, which responded to antihistamines. No allergic reactions were observed in autologous fat groups.

3.4.2 Management and Prognosis of Complications

Most complications (92.7%) were mild to moderate and resolved with conservative treatment (antibiotics, antihistamines, massage, warm compresses). Severe complications (vascular embolism, n=3) were managed with hyaluronidase injection (HA group) or emergency decompression (autologous fat group), with no permanent sequelae (e.g., skin necrosis, blindness) reported. The overall complication resolution rate was 98.4%, with no significant difference in prognosis between the two materials (P = 0.41).

4. Discussion

4.1 Interpretation of Core Results

4.1.1 Comparative Advantages in Contour Fixation Efficacy

The systematic synthesis of 23 studies reveals distinct efficacy characteristics between hyaluronic acid (HA) and autologous fat in facial ligament reinforcement, rooted in their inherent material properties. HA demonstrates superior immediate support, with 92% of included studies confirming significant contour improvement within 1 week post-injection and optimal efficacy achieved at 1–2 months. This advantage stems from the viscoelastic properties of crosslinked HA hydrogels—modern dual-crosslinked formulations exhibit a storage modulus (G') of 1500–3000 Pa, which matches the mechanical tension required for ligament anchoring, enabling instant correction of soft tissue sagging and contour irregularities. Particularly in contour symmetry, HA achieved a significantly higher physician evaluation score (3.7 ± 0.4 vs. 3.3 ± 0.5, P = 0.02), making it the preferred choice for patients seeking precise, rapid aesthetic enhancement.

In contrast, autologous fat exhibits superior long-term tissue integration. Although its optimal efficacy is delayed until 3–6 months post-injection (attributed to fat absorption and tissue remodeling), it outperforms HA in sustained structural improvement. Objective ultrasound measurements showed that autologous fat increased zygomatic ligament thickness by 51.7% ± 10.2% at 18 months, significantly higher than HA's 42.3% ± 9.5% (P = 0.01). This is mediated by the regenerative potential of adipose-derived stem cells (ADSCs) within autologous fat grafts—ADSCs secrete VEGF, EGF, and TGF-β, which promote angiogenesis, collagen synthesis, and ligament tissue remodeling, transforming the injected material into a functional component of the ligament-soft tissue complex rather than a temporary filler. Additionally, autologous fat's superior improvement in skin elasticity (38.5% ± 9.1% vs. 35.2% ± 8.3% increase in R2 value, P = 0.03) reflects its ability to restore tissue vitality beyond mere mechanical support.

4.1.2 Mechanisms Underlying Differences in Duration of Effect

The significant difference in duration of effect (HA: 14.2 ± 3.5 months; autologous fat: 22.6 ± 4.8 months, P < 0.001) is governed by distinct metabolic and survival mechanisms. HA's duration is primarily determined by crosslinking density and molecular weight—dual-crosslinked HA with a crosslinking degree ≥30% and molecular weight >2000 kDa exhibits a mean duration of 19.3 ± 2.5 months, nearly twice that of single-crosslinked HA (9.7 ± 2.1 months, P < 0.001). This is because crosslinking forms a three-dimensional network that resists degradation by hyaluronidase in the extracellular matrix, with degradation rate inversely

proportional to crosslinking density. However, HA remains a temporary implant, and gradual enzymatic hydrolysis ultimately leads to efficacy attenuation, with only 38.5% of initial effect retained at 24 months.

Autologous fat's long-term durability relies on cellular survival and regenerative integration. Studies using DAM-assisted purification or VASER liposuction achieved fat survival rates ≥70%, corresponding to a mean duration of 28.5 ± 3.2 months—significantly longer than survival rates <60% (17.3 ± 2.8 months, $P < 0.001$). Surviving adipocytes establish stable vascular connections with the host tissue, persisting as functional components for years, while ADSC-mediated collagen deposition continuously reinforces ligament density. This "living implant" characteristic explains why autologous fat maintains 65.3% of its efficacy at 24 months, far exceeding HA's 38.5% ($P < 0.001$). Subgroup analysis further confirms that patient age (<45 years) and deep-layer injection (ligament-bone attachment point) enhance duration for both materials, as younger skin's higher elasticity and deep anatomical positioning reduce mechanical stress on the injected material.

4.2 Clinical Decision-Making Recommendations

4.2.3 Patient-Tailored Material Selection

Clinical selection should be guided by individual patient characteristics to balance efficacy, durability, and aesthetic goals:

Age: Patients <45 years with mild-to-moderate ligament laxity and high skin elasticity benefit from HA, as its immediate effect aligns with short-term aesthetic needs and avoids the recovery period associated with fat harvesting. Patients >50 years with severe sagging and reduced tissue vitality prefer autologous fat, as its regenerative properties address both ligament support and skin quality improvement.

Laxity severity: HA is suitable for mild-to-moderate laxity (soft tissue displacement <3 mm), providing targeted support without overcorrection. Severe laxity (>4 mm displacement) requires autologous fat's stronger long-term anchoring, or combined treatment (HA for immediate correction + autologous fat for sustained reinforcement).

Aesthetic preferences: Patients seeking natural, gradual improvement opt for autologous fat, as its remodeling process avoids the "artificial" contour associated with excessive HA. Those desiring precise, predictable results (e.g., mandibular margin refinement) choose HA, whose viscoelasticity enables controlled shaping.

Economic considerations: HA has a lower initial cost ($800–$1500 per session) but requires touch-ups every 12–18 months. Autologous fat has a higher upfront cost ($2000–$3500) but reduces long-term expenses, with cost-effectiveness surpassing HA after 2 years of follow-up.

4.2.4 Injection Technique Optimization

Precision in injection parameters directly impacts efficacy and duration:

Target localization: Ultrasound-guided injection ensures material delivery to the ligament core—zygomatic ligament injection at 1/3 of the lateral canthus-earlobe line, masseteric ligament at 1 cm anterior to the masseter muscle insertion, and mandibular ligament at the mandibular angle. Blind injection increases the risk of material deposition in subcutaneous tissue, reducing support efficacy by 30% (as shown in 3 included studies).

Dose control: Optimal dose ranges from 0.3–0.8 mL per ligament for HA (dual-crosslinked) and 0.5–1.2 mL for autologous fat. Excessive volume (>1.5 mL) increases nodule formation risk (HA: 1.8% → 3.5%; autologous fat: 3.2% → 5.7%), while insufficient dose (<0.2 mL) leads to inadequate support with duration reduced by 40%.

Injection technique: Retrograde linear injection for HA ensures uniform distribution along the ligament, while autologous fat requires a 4-layer injection (submuscular to subcutaneous) to maximize contact with vascular networks, improving survival rate by 15–20% compared to single-layer injection.

4.3 Limitations of Current Research

Despite the comprehensive literature synthesis, this review acknowledges several limitations inherent to the existing evidence base:

Heterogeneity: Significant heterogeneity exists in material parameters (HA crosslinking degree: 18–35%; fat processing methods: centrifugation, VASER, DAM), efficacy indicators (subjective scales vs. objective measurements), and follow-up durations (6 months–3 years), leading to moderate heterogeneity (I^2=68%, $P<0.001$) in the duration analysis. This variability limits the generalizability of pooled results and hinders direct comparison between studies.

Insufficient RCT evidence: Only 5 of the 23 included studies are RCTs, with most being single-arm cohort studies or case series. No large-sample (n>100), long-term (≥3 years) head-to-head RCTs exist, resulting in low-to-moderate evidence quality for efficacy comparisons.

Bias and subjective evaluation: Retrospective studies (n=6) exhibit selection bias, as patients with better baseline characteristics are more likely to be included. Subjective outcome measures (GAIS, VAS) lack blinding in 12 studies, leading to overestimation of efficacy by 10–15%. Objective indicators (ligament thickness, soft tissue displacement) are inconsistently measured across studies, with only 4 studies using standardized 3D facial scanning.

Incomplete safety data: Long-term complications (>1 year) are underreported—only 3 studies document late nodules or fat necrosis, and no studies assess the risk of ligament fibrosis or chronic inflammation, limiting the understanding of long-term safety profiles.

4.4 Future Research Directions

Addressing current gaps requires targeted research to strengthen the evidence base and advance clinical practice:

Standardized head-to-head RCTs: Future studies should adopt uniform protocols—fixed HA parameters (crosslinking degree 30%, molecular weight 2000 kDa), standardized fat processing (VASER + centrifugation at 3000 rpm for 5 min), and consistent outcome measures (3D scanning for soft tissue displacement, ultrasound for ligament thickness, and blinded GAIS evaluation at 6, 12, and 24 months). Sample sizes ≥150 per group will enhance statistical power to detect small differences in duration and safety.

Material modification: Developing long-acting HA via novel crosslinking technologies (e.g., click chemistry) to extend degradation to 3 years without compromising biocompatibility. Enhancing autologous fat survival through ADSC enrichment (1×10^6 cells/mL) or platelet-rich plasma (PRP) co-injection—preliminary studies show ADSC-assisted fat grafting increases survival rate by 25% and duration by 8 months.

Objective evaluation tools: Developing specialized devices to measure ligament support force (e.g., biomechanical tension meters) and 4D facial imaging (capturing dynamic movements) to replace subjective scales. Validating these tools against anatomical gold standards (cadaveric studies) will improve outcome reliability.

Multicenter, long-term studies: Conducting international multicenter trials to reduce regional bias in injection techniques and patient populations. Extending follow-up to 5 years will clarify long-term durability, particularly autologous fat's regenerative sustainability and HA's cumulative safety with repeated injections. Additionally, exploring personalized medicine—genetic markers predicting fat survival or HA degradation rate—could enable precision treatment planning.

5. Conclusions

This systematic review comprehensively synthesizes evidence from 23 clinical studies to compare the efficacy, duration of effect, and safety of hyaluronic acid (HA) and autologous fat in facial ligament reinforcement, providing evidence-based guidance for clinical practice and future research.

In terms of contour fixation efficacy, HA and autologous fat exhibit distinct complementary characteristics. HA delivers superior immediate support and precise contouring, achieving significant aesthetic improvement within 1 week post-injection and optimal symmetry correction at 1–2 months, attributed to its tailored viscoelastic properties. Autologous fat, by contrast, offers prominent long-term tissue integration and regenerative advantages, with gradual improvement over 3–6 months and sustained ligament thickening (51.7% vs. HA's 42.3% at 18 months) driven by adipose-derived stem cell-mediated tissue remodeling. Regarding duration of effect, autologous fat demonstrates a statistically significant advantage (22.6 ± 4.8 months vs. 14.2 ± 3.5 months, $P < 0.001$), maintaining 65.3% of its efficacy at 24 months compared to 38.5% for HA. Safety profiles are favorable for both materials: HA has a lower overall complication rate (10.7% vs. 16.3%, $P < 0.001$), primarily associated with transient allergic reactions (0.2%) and mild nodules (1.8%), while autologous fat carries a higher risk of post-procedural swelling/bruising (12.5%) and late nodules (3.2%) but avoids immunogenicity.

The clinical application of these two materials should be individualized based on patient characteristics and treatment goals. HA is recommended for patients under 45 years with mild-to-moderate ligament laxity, who prioritize immediate results, precise contour refinement, and minimal recovery time—particularly those seeking short-term aesthetic enhancement or correction of focal contour irregularities. Autologous fat is preferred for patients over 50 years with severe laxity and reduced tissue vitality, as well as those desiring long-term, natural-looking rejuvenation, given its regenerative benefits for skin elasticity and cost-effectiveness over 2 years of follow-up. Injection technique optimization, including ultrasound-guided targeted delivery, dose control (0.3–0.8 mL/ligament for HA, 0.5–1.2 mL/ligament for autologous fat), and appropriate injection layers, is critical to maximizing efficacy and minimizing complications for both materials.

Despite the value of the synthesized evidence, current research is limited by moderate heterogeneity, insufficient large-sample head-to-head RCTs, and subjective outcome evaluation. Future research should prioritize standardized RCTs with uniform material parameters, consistent objective measurement tools (e.g., 3D facial scanning, ligament tension meters), and long-term (≥3 years) follow-up to clarify comparative effectiveness. Additionally, exploring material modifications (e.g., long-acting crosslinked HA, adipose-derived stem cell-enriched fat grafts) and developing personalized treatment strategies based on patient age, tissue status, and genetic markers will further advance the precision and durability of facial ligament reinforcement.

In summary, HA and autologous fat are both effective and safe for facial ligament reinforcement, with HA excelling in immediate, precise contouring and autologous fat in long-term, regenerative support. Tailored material selection based on individual patient needs, combined with optimized injection techniques, will achieve optimal facial rejuvenation outcomes. Addressing current research gaps through high-quality clinical trials will continue to strengthen the evidence base for this important aesthetic intervention.

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