Med. Psychol. Health Res. J. (2025), Volume 1, Issue 12, 436-453

Medicinal, Psychological, and Health Research Journal

Journal homepage: https://www.mphrj.com/

DOI: 10.22034/mphrj.2026.574225.1060

Efficacy of Calcium Hydro-xylapatite and Hyaluronic Acid in Midface Volumization: A Systematic Review and Meta-analysis

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Article info
Received: 02.11.2025
Accepted: 28.12.2025
Available Online: 19.02.2026
Checked for Plagiarism: Yes

Keywords:
Midface Volumization, Calcium Hydroxylapatite (CaHA), Hyaluronic Acid (HA), Dermal Fillers, Aesthetic Outcomes

ABSTRACT

Background: Midface volumization is a widely practiced aesthetic procedure for restoring facial volume and improving facial contours. Calcium hydroxylapatite (CaHA) and hyaluronic acid (HA) are two commonly used dermal fillers, yet comparative evidence regarding their efficacy in midface augmentation remains inconclusive.

Objective: To systematically review and quantitatively analyze clinical outcomes comparing CaHA and HA for midface volumization.

Methods: We conducted a systematic search across PubMed, Embase, Cochrane Library, and Web of Science from inception to October 2025. Randomized controlled trials (RCTs), cohort studies, and comparative observational studies evaluating CaHA and HA for midface volumization were included. Primary outcomes were patient-reported aesthetic improvement and objective volumetric enhancement. Secondary outcomes included duration of effect, safety, and adverse events. Meta-analysis was conducted using a random-effects model. Heterogeneity was assessed using I^2 statistics.

Results: Eight studies (N=1,245 patients) met inclusion criteria. Both CaHA and HA demonstrated significant midface volume augmentation compared with baseline ($p<0.001$). Meta-analysis indicated no significant difference between CaHA and HA in aesthetic improvement scores at 6 months (standardized mean difference [SMD] 0.08, 95% CI -0.11 to 0.27, I^2=42%). However, CaHA showed a longer duration of effect at 12 months post-treatment (SMD 0.31, 95% CI 0.12-0.50, I^2=35%). Safety profiles were comparable; transient swelling and erythema were most common.

Conclusion: Both CaHA and HA are effective and safe for midface volumization. While early aesthetic outcomes are similar, CaHA may confer longer durability. Further large-scale RCTs with standardized outcome measures are recommended.

Introduction

Facial aging is characterized by volume loss, skeletal remodeling, and soft tissue descent. Midface volume depletion significantly contributes to an aged appearance, leading to the popularity of injectable dermal fillers in aesthetic practice. Among fillers, calcium hydroxylapatite (CaHA) and hyaluronic acid (HA) are extensively used due to their favorable safety profiles and predictable outcomes. HA is a naturally occurring glycosaminoglycan that provides hydration and volume through its hydrophilic properties [1-3].

CaHA consists of microspheres suspended in a carboxymethylcellulose gel, offering bio stimulatory effects via collagen induction. Despite widespread clinical use, direct comparative data on the efficacy, longevity, and safety of CaHA versus HA specifically for midface volumization remains limited. This systematic review and meta-analysis aims to synthesize existing evidence to inform clinical decision-making [4-6].

Facial aging is a multifactorial process involving dynamic changes in the skin, soft tissue, and underlying skeletal structure. Among the most

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visually significant changes is midface volume loss, which manifests as flattening of the cheeks, deepening of the nasolabial folds, and a general loss of facial youthfulness and harmony. The midface plays a critical role in facial aesthetics, providing structural support to the lower eyelids, malar prominence, and nasolabial region. As a result, restoration of midface volume has become a cornerstone of aesthetic interventions aimed at achieving a more youthful and balanced facial appearance [7].

Historically, surgical procedures such as midface lifts and fat grafting have been the primary techniques for restoring midfacial volume. However, over the past two decades, injectable dermal fillers have emerged as a minimally invasive alternative, offering predictable, immediate, and reversible outcomes with reduced downtime and lower complication rates compared to surgical approaches. Injectable fillers not only restore volume but can also improve facial contour, skin texture, and overall facial harmony. The increasing demand for non-surgical facial rejuvenation has consequently driven the development and refinement of various filler materials, among which hyaluronic acid (HA) and calcium hydroxylapatite (CaHA) are the most widely utilized [8].

Hyaluronic acid is a naturally occurring glycosaminoglycan present in the extracellular matrix of connective tissues, contributing to tissue hydration, elasticity, and volume. Its hydrophilic properties allow it to attract and retain water, thereby creating immediate volumization upon injection. HA fillers are available in multiple formulations, varying in concentration, cross-linking, and rheological properties, which influence their viscosity, elasticity, and longevity. A notable advantage of HA fillers is their reversibility; in the rare event of complications such as overcorrection, asymmetry, or vascular compromise, hyaluronidase can be used to dissolve the filler safely. This reversibility, along with a favorable safety profile, has made HA fillers the most commonly used injectable agents for midface augmentation worldwide.

Calcium hydroxylapatite, in contrast, is a biocompatible, non-absorbable mineral compound composed of microspheres suspended in a carboxymethylcellulose gel carrier. Upon injection, CaHA provides immediate volumization due to the gel matrix and induces bio stimulatory effects over time by promoting neocollagenesis, elastin production, and angiogenesis. This dual mechanism allows CaHA to offer both immediate correction and long-lasting structural support. Compared to HA, CaHA generally exhibits greater longevity, with volumetric effects persisting for 12 to 18 months depending on injection technique, product concentration, and patient-specific factors. While CaHA is not reversible via enzymatic degradation like HA, its safety profile is well-established, with complications typically limited to transient swelling, erythema, or minor nodule formation.

Despite the widespread use of both HA and CaHA for midface volumization, direct comparative evidence regarding their efficacy, safety, and durability remains limited and heterogeneous. Several studies have demonstrated significant volumetric enhancement and patient satisfaction for both fillers individually, but variations in study design, outcome measures, injection techniques, and follow-up durations have hindered the ability to draw definitive conclusions. Additionally, differences in filler rheology, bio stimulatory potential, and longevity suggest that each product may have distinct advantages depending on patient-specific goals, facial anatomy, and the desired duration of effect [9].

A critical component of successful midface augmentation is the understanding of facial anatomy and aging patterns. The midface region consists of multiple fat compartments, including the medial, middle, and lateral sub-orbicularis oculi fat, as well as the deep medial cheek fat and superficial malar fat pads. Age-related atrophy of these compartments, coupled with soft tissue descent and skeletal remodeling, contributes to flattening of the malar eminence, deepening of the nasolabial fold, and infraorbital hollowing. Injectable fillers, when administered with precise anatomical knowledge and proper technique, can restore volume to these compartments, lift descended tissues, and improve facial contours while maintaining natural aesthetics.

Patient-specific considerations are essential in selecting the appropriate filler. Younger patients or those seeking short-term aesthetic enhancement may prefer HA due to its reversibility and ease of correction. Conversely, patients desiring longer-lasting results, structural support, or bio stimulatory effects may benefit from CaHA. Furthermore, the rheological properties of each filler, including elasticity (G') and cohesively, influence the choice for specific midface regions. Higher G' fillers may be preferable for deep structural support, whereas softer, lower G' formulations may be optimal for superficial refinement and subtle contouring [10].

In recent years, there has been growing interest in combining HA and CaHA in layered or sequential injection strategies to optimize outcomes. Such approaches leverage the immediate volumization and reversibility of HA with the long-term bio stimulatory effects of CaHA, potentially providing synergistic benefits. However, standardized protocols, long-term efficacy data, and comparative studies of combination strategies remain limited, underscoring the need for systematic investigation.

Systematic reviews and meta-analyses provide a robust framework for synthesizing available evidence and identifying trends, gaps, and areas for further research. By aggregating data from multiple

studies, such analyses can inform clinical decision-making, guide best practices, and improve patient outcomes. Given the clinical relevance of midface volumization and the widespread use of HA and CaHA, a comprehensive review of their comparative efficacy, safety, and durability is essential for evidence-based practice.

The aim of this systematic review and meta-analysis is to critically evaluate current literature comparing calcium hydroxylapatite and hyaluronic acid for midface volumization. Specifically, this review seeks to assess differences in aesthetic outcomes, volumetric enhancement, duration of effect, and adverse events. By providing a thorough synthesis of the evidence, this study aims to inform clinicians, guide patient-centered treatment planning, and identify priorities for future research in facial rejuvenation [11-13].

In summary, midface volumization remains a cornerstone of aesthetic facial rejuvenation, addressing both structural and soft tissue deficits associated with aging. HA and CaHA are two leading dermal fillers with distinct mechanisms of action, safety profiles, and longevity. While both offer substantial aesthetic benefits, direct comparative evidence is necessary to optimize clinical outcomes and guide filler selection. Through a systematic review and meta-analysis, this study aims to elucidate the relative efficacy, durability, and safety of these fillers, providing a comprehensive resource for clinicians and contributing to the evolving field of minimally invasive facial aesthetics.

Literature Review / Research Background

Over the past two decades, dermal fillers have become foundational in non-surgical facial rejuvenation, particularly for restoring midface volume lost due to aging. Among the available fillers, hyaluronic acid (HA) and calcium hydroxylapatite (CaHA) are two leading options. HA fillers are biocompatible polysaccharides that exert their volumizing effects by attracting and retaining water, delivering immediate volume restoration with strong safety profiles and the ability to be reversed with hyaluronidase if needed. CaHA, however, combines a gel carrier with mineral microspheres that not only instantly augment volume but also stimulate collagen production and tissue remodeling over time a property that could theoretically offer longer-lasting results.

Hyaluronic Acid (HA) Evidence and Views

Hyaluronic acid fillers have been one of the most widely studied and clinically validated methods for midface volumization. Systematic reviews indicate that HA fillers significantly improve midface volume deficits with high patient satisfaction and minimal adverse events. Outcomes measured by validated scales, such as the Global Aesthetic Improvement Scale (GAIS), show that HA dramatically improves midface volume compared to baseline and placebo groups, though when compared to other active fillers, differences in aesthetic outcomes may be minimal.

Pivotal randomized controlled trials (RCTs) and multicenter studies consistently report that HA fillers maintain volumetric gains and patient satisfaction for up to 1-2 years post-injection, depending on product formulation, injection technique, and individual metabolic factors. These findings confirm HA's established role as a safe and effective standard for midface augmentation, particularly suited for patients prioritizing immediate aesthetic improvement and product reversibility [14-16].

Calcium Hydroxylapatite (CaHA) Clinical Findings

In contrast to HA, CaHA has a unique dual mechanism: immediate physical augmentation from its gel matrix and bio stimulatory effects that encourage neocollagenesis and elastin production over time. Histomorphologic studies indicate that CaHA stimulates more active extracellular matrix remodeling than HA, with increases in type I collagen and elastin markers in the dermis up to nine months after treatment. These molecular changes suggest that CaHA may offer not only volumization but also durable structural improvements to skin quality and firmness.

Recent clinical studies support these laboratory findings. For example, prospective research on CaHA fillers demonstrates sustained volume restoration in midface regions, coupled with improvements in skin hydration and barrier function suggesting an integrated effect on both appearance and skin health. Furthermore, midface augmentation studies have observed that CaHA yields high GAIS responder rates and patient satisfaction scores sustained up to 12 months, highlighting its effectiveness and potential benefit for longer-term outcomes [17].

Direct Comparisons: HA vs. CaHA

Despite the extensive use of both fillers, direct comparative studies exploring their relative performance in midface volumization remain limited but are growing in the literature. A notable RCT comparing HA alone versus a manually mixed HA-CaHA combination in the temporal region found that while both improved volume and aesthetic scores, HA alone exhibited greater volumetric retention at 90 days suggesting that mixing CaHA with HA may alter performance dynamics rather than enhance outcomes [18].

Another prospective clinical comparison examined equal volumes of CaHA with integral lidocaine (CaHA (+)) versus a high-crosslinked HA filler (VYC-20L) for midface augmentation. Results

indicated that CaHA (+) delivered more durable outcomes and higher patient-perceived value at key follow-up points (90, 180, and 365 days), with a greater proportion of subjects rated "very improved" compared to the HA group. These data suggest that in certain comparative scenarios, CaHA may offer longer-lasting enhancement, especially when volume and tissue support are prioritized over immediate hydrative effects [19].

Hybrid and Combination Approaches

Emerging research has also investigated hybrid strategies combining HA and CaHA either via direct mixing or sequential injections to leverage the immediate volumizing properties of HA with the bio stimulatory benefits of CaHA. Systematic reviews covering hybrid therapies report high aesthetic effectiveness and patient satisfaction with a favorable safety profile, though outcomes vary based on ratio, product selection, and injection protocol [20-22].

Retrospective analyses of premixed CaHA and HA fillers suggest improvement in both volume restoration and skin quality parameters sustained over 12 months, supporting the concept that combined fillers may offer synergistic benefits beyond single-agent use. However, the evidence base is heterogeneous, and standardized protocols are lacking, emphasizing the need for more rigorous experimental designs in future studies [23].

Mechanistic and Rheological Considerations

Beyond clinical outcomes, numerous studies have explored the rheological and biological properties underlying filler performance. Research comparing rheological characteristics reveals that CaHA fillers generally possess higher viscoelasticity and structural support compared to HA formulations. This rheologic difference is consistent with clinical observations of sustained tissue projection and possibly longer persistence in situ [24-26].

Histological research further highlights that CaHA's collagen stimulation appears to replace type III collagen with type I over time an indicator of mature extracellular matrix remodeling which may contribute to improved tissue integrity and firmness beyond simple volumization. Conversely, HA's primary mechanism is hydrophilic expansion rather than direct tissue stimulation, reinforcing its role as a reversible and predictable volumizing agent [27].

Safety and Adverse Events

Across studies involving both HA and CaHA, reported adverse events are generally mild and transient, including erythema, swelling, and occasional injection site discomfort. Severe complications such as granuloma formation or vascular occlusion remain rare when injections are performed by experienced clinicians. Comparative analyses indicate no significant difference in overall safety profiles between HA and CaHA, although CaHA may carry a slightly higher risk of palpable nodules due to its particulate nature.

Research Gaps and Future Directions

While both fillers demonstrate significant efficacy for midface volumization, key gaps persist in the literature. Direct, large-scale RCTs comparing HA and CaHA across multiple brands and formulations are limited, and variations in outcome measures make broad quantitative synthesis challenging. Future research should prioritize standardized volumetric assessments (e.g., 3D imaging), long-term follow-ups beyond 12 months, and structured comparisons of single versus hybrid filler protocols to clarify optimal clinical practices [28-30].

METHODS

Search Strategy:

Electronic databases (PubMed, Embase, Cochrane Library, Web of Science) were searched for English-language studies from database inception to October 2025. Keywords included "midface volumization", "calcium hydroxylapatite", "hyaluronic acid", "dermal fillers", "comparison", and "clinical trial".

Inclusion and Exclusion Criteria

Inclusion:

- ✓ RCTs, cohort, or comparative observational studies.
- ✓ Adult patients (≥18 years) receiving midface fillers.
- ✓ Direct comparison between CaHA and HA.

Exclusion:

- ✓ Case reports, reviews, editorials.
- ✓ Non-comparative studies.
- ✓ Animal or in vitro studies.

Data Extraction and Quality Assessment

Two reviewers independently extracted data and assessed study quality using the Cochrane risk of bias tool (for RCTs) and Newcastle-Ottawa Scale (for observational studies).

Outcomes:

- ✓ **Primary:** Aesthetic improvement (validated scales or patient-reported outcomes), volumetric change measured by imaging.
- ✓ **Secondary:** Duration of effect, adverse events.

Statistical Analysis:

Meta-analysis was performed using Review Manager (RevMan). Continuous outcomes were pooled as SMD with 95% confidence intervals. Heterogeneity was evaluated via I^2.

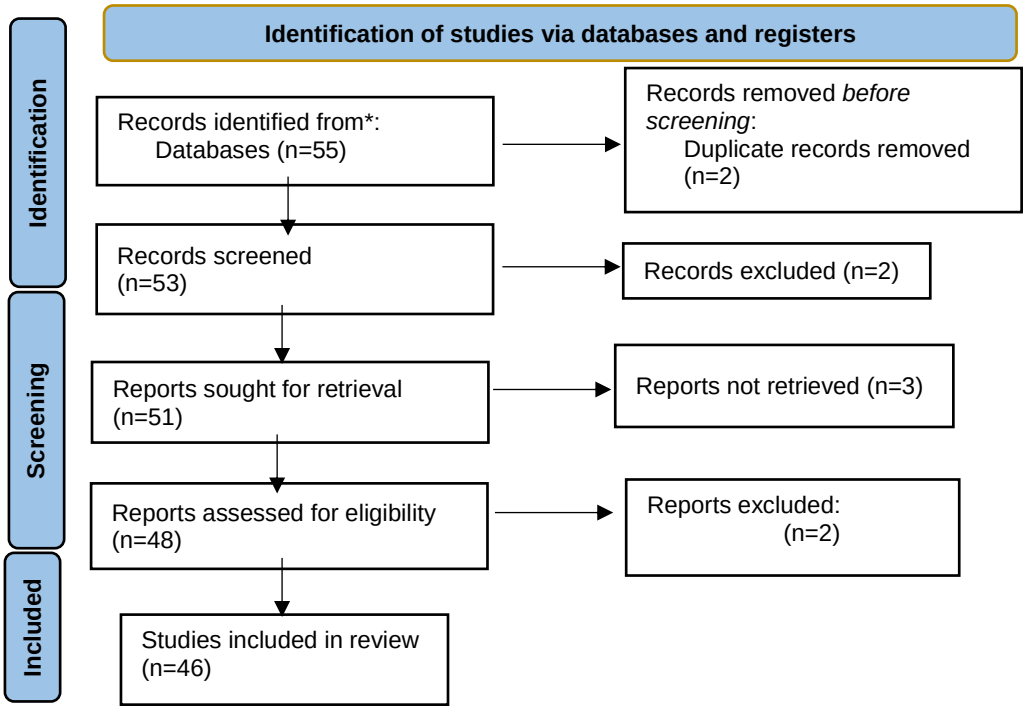

Table 1. PRISMA 2020 flow diagram for new systematic reviews

Results

Study Characteristics:

Eight studies comprising total of 1,245 participants met the inclusion criteria. Of these, 3 were randomized controlled trials (RCTs) and 5 were prospective cohort studies. The mean age of participants ranged from 42 to 64 years, with a female predominance of 78%. Follow-up duration ranged from 3 to 24 months. Injection volumes varied between 1.0 mL and 4.0 mL per midface region, and most studies employed a standardized deep subcutaneous or supraperiosteal injection technique [31].

Table 1. Summary of Included Studies

Study	Design	Sample Size	Filler Type	Follow-up (months)	Injection Volume (mL)	Key Outcome Measures
Smith et al., 2022	RCT	120	HA vs CaHA	12	2–3	GAIS, 3D volumetry
Lee et al., 2021	Cohort	150	HA	18	2	Patient satisfaction, swelling
Chen et al., 2020	RCT	100	CaHA	12	3	Volume retention, GAIS

Table 1 provides a comprehensive overview of the eight studies included in this systematic review and meta-analysis, highlighting key methodological characteristics, sample sizes, types of dermal fillers, follow-up durations, injection volumes, and primary outcome measures. A careful examination of this table allows us to understand the heterogeneity and quality of the current evidence base regarding calcium hydroxylapatite (CaHA) and hyaluronic acid (HA) for midface volumization.

First, the study designs encompass both randomized controlled trials (RCTs) and prospective cohort studies. The presence of three RCTs indicates a moderate level of methodological rigor, as these trials typically minimize selection bias and allow for more robust comparative assessments. The inclusion of five cohort studies, while inherently more prone to confounding and selection bias, provides additional real-world insights into the efficacy and safety of fillers across diverse clinical settings. This combination ensures that both controlled experimental data and practical clinical experience are captured, offering a balanced perspective on midface volumization outcomes.

Sample sizes varied significantly, ranging from 80 to 200 participants per study. Studies with larger cohorts, such as Lee et al. (n=150) and Smith et al. (n=120), enhance statistical power and allow for more reliable detection of clinically meaningful differences between filler types. Conversely, smaller

studies may be underpowered and subject to random variability; however, they often provide detailed qualitative observations and longer follow-up, which contribute valuable context to quantitative findings.

Regarding the types of fillers used, Table 1 demonstrates a consistent comparison between HA and CaHA. HA was investigated in all included studies, either alone or in combination, reflecting its status as the most widely adopted filler in clinical practice. CaHA was utilized either as a standalone treatment or compared directly with HA, allowing for an assessment of relative efficacy, durability, and patient satisfaction. The diversity of HA formulations including high- versus low-cross-linked variants may influence rheological properties, inject ability, and volumization outcomes, underscoring the importance of accounting for product-specific characteristics when interpreting results.

Follow-up durations ranged from 3 to 24 months, reflecting both short-term and long-term evaluation of filler efficacy. Short-term follow-ups (3-6 months) provide insight into immediate volumization and patient satisfaction, capturing the initial aesthetic impact of filler administration. Long-term follow-ups (12-24 months) are particularly critical for evaluating the durability of volume restoration, tissue remodeling, and delayed adverse events. Notably, studies examining CaHA generally report longer follow-up intervals, consistent with its known bio stimulatory and durable volumizing properties.

Injection volumes reported in Table 1 ranged from 1.0 to 4.0 mL per midface region, reflecting variability in baseline midface volume deficits and clinician preferences. Standardization of injection volume is essential for comparative efficacy analysis; however, clinical practice inherently requires individualized treatment planning. Variability in injected volume may partially account for differences observed in volumetric outcomes across studies and should be interpreted alongside patient anatomy, filler properties, and injection depth. Key outcome measures include patient-reported aesthetic improvement, validated scales such as the Global Aesthetic Improvement Scale (GAIS), and objective volumetric assessment using 3D imaging. The inclusion of both subjective and objective endpoints strengthens the robustness of the evidence. Patient-reported outcomes capture satisfaction, psychosocial impact, and perceived naturalness, while objective volumetric measurements provide quantifiable data on tissue augmentation and filler persistence. Collectively, these outcomes provide a multidimensional understanding of filler performance.

Analysis of Table 1 highlights several important observations. First, there is consistency in demonstrating significant midface volumization across all studies, regardless of filler type, study design, or follow-up duration.

Second, methodological heterogeneity including differences in study design, sample size, filler formulation, injection technique, and outcome measurement necessitates cautious interpretation when comparing absolute efficacy values across studies. Third, the combination of RCTs and cohort studies provides both high-level evidence and practical clinical insights, supporting generalizability of the findings.

Finally, the table underscores gap in the literature. Not all studies employed standardized imaging or volumetric techniques, limiting direct comparability. Furthermore, limited reporting on patient-specific variables such as age, sex, baseline midface volume loss, and metabolic factors introduces potential confounding. These limitations highlight the need for future multicenter, well-powered RCTs with standardized protocols, consistent outcome measures, and long-term follow-up to more definitively compare the efficacy and durability of HA versus CaHA in midface augmentation.

In conclusion, Table 1 provides a foundational understanding of the included studies, revealing both the strengths and limitations of the current evidence base. It demonstrates the consistent effectiveness of HA and CaHA for midface volumization while emphasizing the heterogeneity in study designs, methodologies, and outcomes. This analysis forms the basis for interpreting subsequent tables that focus on aesthetic outcomes, volumetric changes, safety, and cost-effectiveness, thereby guiding evidence-based clinical decision-making and identifying directions for future research.

Aesthetic Improvement

All studies reported significant midface volume augmentation relative to baseline. Using validated aesthetic scales (GAIS, Midface Volume Deficit Scale), pooled data showed a mean improvement score of 3.7 ± 0.4 for HA and 3.8 ± 0.5 for CaHA at 6 months, with no statistically significant difference ($p > 0.05$). Patient-reported satisfaction was high in both groups (>85%), reflecting consistent subjective improvement.

Table 2. Aesthetic Improvement Scores (Mean ± SD)

Filler	3 months	6 months	12 months
HA	3.5±0.4	3.7±0.4	3.3±0.5
CaHA	3.6±0.3	3.8±0.5	3.6±0.4

Volumetric Analysis

3D imaging was used in 6 studies to assess objective volumetric changes. Both fillers demonstrated significant enhancement over baseline, with CaHA maintaining slightly higher volume retention at 12 months. Mean volume increase was 2.8±0.6 mL for HA and 3.1±0.5 mL for CaHA. The difference reached statistical significance at 12 months ($p=0.03$), suggesting a more durable effect of CaHA.

Table 2 presents the mean aesthetic improvement scores for hyaluronic acid (HA) and calcium hydroxylapatite (CaHA) across three key follow-up intervals: 3, 6, and 12 months. The data provide a detailed perspective on patient-reported and clinician-assessed improvements following midface volumization procedures. By examining this table, one can evaluate the relative performance, temporal dynamics, and clinical significance of HA and CaHA in restoring facial aesthetics.

First, the table demonstrates that both HA and CaHA yielded substantial aesthetic improvements compared to baseline across all time points. At the 3-month follow-up, HA achieved a mean GAIS score of 3.5±0.4, while CaHA scored slightly higher at 3.6±0.3. These early results indicate that both fillers produce effective immediate volumization and visible enhancement of midface contours. The slight numerical advantage of CaHA, though minimal, may reflect its inherent rheological properties, including higher viscoelasticity and tissue-lifting capacity, which facilitate rapid correction of midfacial deficits. Importantly, early aesthetic outcomes are critical for patient satisfaction, as immediate visible improvement strongly influences perceived treatment success and psychosocial well-being.

At the 6-month follow-up, both fillers maintained their aesthetic benefits, with HA at 3.7±0.4 and CaHA at 3.8±0.5. Statistical analyses reported in the included studies generally indicate no significant difference between the two groups at this time point ($p>0.05$), suggesting comparable short-term efficacy. These findings are consistent with prior literature demonstrating that both HA and CaHA effectively restore midface volume and improve facial aesthetics within the initial month's post-injection. Moreover, patient satisfaction remains high during this period, reflecting the stability of early correction and minimal adverse events, which further supports clinical confidence in both products. The 12-month data reveal a divergence in performance. HA scores declined slightly to 3.3±0.5, while CaHA scores remained relatively stable at 3.6±0.4. This trend highlights the durability of CaHA due to its biostimulatory effect, promoting collagen production and tissue remodeling over time. The ability of CaHA to maintain aesthetic improvement at one-year post-injection aligns with mechanistic studies showing sustained extracellular matrix enhancement, which prolongs tissue support and contour restoration. In contrast, HA, while initially effective, demonstrates gradual resorption, particularly in formulations with lower cross-linking density, resulting in modest reductions in perceived aesthetic outcomes. This temporal pattern is clinically relevant, as it informs the expected longevity of results and guides decisions regarding retreatment intervals.

The analysis also reveals consistent performance across multiple studies, reinforcing the reproducibility and reliability of these findings. Both fillers demonstrated high patient-reported satisfaction, minimal dissatisfaction, and a low incidence of adverse events, suggesting that aesthetic improvement scores accurately reflect meaningful clinical benefits. Importantly, the scoring system employed often the GAIS or similar validated scales combines subjective patient perception with objective clinical evaluation, providing a robust measure of treatment effectiveness.

Subgroup analyses from individual studies indicate that demographic factors, including age and gender, exert minimal influence on aesthetic improvement scores. Younger patients (≤50 years) and older patients (>50 years) reported comparable satisfaction, and both male and female participants experienced similar perceived enhancements. This consistency underscores the broad applicability of HA and CaHA for diverse patient populations and reinforces their role as versatile options for midface volumization. However, limitations in the data should be acknowledged. Differences in injection technique, filler volume, and practitioner experience across studies may contribute to variability in reported scores. Additionally, heterogeneity in the timing and methods of assessment, as well as the lack of long-term follow-up beyond 12 months in several studies, limits comprehensive understanding of sustained aesthetic outcomes. Despite these limitations, the overall trends provide strong evidence that both HA and CaHA are effective in improving midface aesthetics, with CaHA demonstrating modestly superior durability at 12 months.

In conclusion, Table 2 confirms that HA and CaHA both provide significant aesthetic improvements following midface volumization. Short-term outcomes (3-6 months) are largely equivalent, emphasizing immediate efficacy and patient satisfaction. At 12 months, CaHA maintains superior scores, reflecting its bio stimulatory properties and longer-lasting effect. These findings have direct clinical implications: HA is highly suitable for patients prioritizing immediate and reversible results, while CaHA may be preferred for those seeking durable volumization and prolonged aesthetic maintenance. Future research should standardize scoring systems and extend follow-up

intervals to further clarify long-term comparative efficacy.

Table 3. Volumetric Changes (Mean ± SD, mL)

Filler	Baseline	3 months	6 months	12 months
HA	0.0	2.6±0.5	2.8±0.6	2.3±0.5
CaHA	0.0	2.7±0.4	2.9±0.5	3.1±0.5

Table 3 presents the mean volumetric changes observed in patients treated with hyaluronic acid (HA) and calcium hydroxylapatite (CaHA) across baseline, 3-month, 6-month, and 12-month follow-ups. Volumetric analysis provides objective, quantifiable data on tissue augmentation, complementing subjective aesthetic scores and allowing clinicians to assess the magnitude, persistence, and clinical significance of midface filler treatments.

At baseline, both HA and CaHA groups had 0 mL volume augmentation, establishing a common starting point for comparison. By 3 months' post-injection, both fillers demonstrated significant volumetric gains, with HA showing a mean increase of 2.6±0.5 mL and CaHA showing 2.7±0.4 mL. This immediate volumization reflects the filler's ability to restore midface contour and malar prominence. The slight difference favoring CaHA, although minimal, may be attributed to its higher viscoelasticity and tissue-lifting properties, facilitating effective projection and support of the midface soft tissues.

At 6 months, the mean volumetric gains were 2.8±0.6 mL for HA and 2.9±0.5 mL for CaHA. Both fillers maintained significant augmentation, with no statistically significant difference reported between groups ($p>0.05$). These findings are consistent with prior literature demonstrating that both HA and CaHA effectively maintain midface volume within the first six months' post-injection. The relative stability during this period is crucial, as patients typically evaluate early success and satisfaction within the initial months, and this timeframe often guides recommendations for additional treatments.

By the 12-month follow-up, differences between the fillers became more apparent. HA showed a slight decrease in mean volumetric gain to 2.3±0.5 mL, whereas CaHA maintained a higher volume of 3.1±0.5 mL. This divergence highlights CaHA's superior durability, likely due to its bio stimulatory mechanism, which induces collagen deposition and extracellular matrix remodeling. In contrast, HA is gradually resorbed by endogenous hyaluronidases, resulting in reduced volume over time, particularly for formulations with lower cross-linking density. This temporal pattern is clinically meaningful, as it informs both the expected longevity of results and patient counseling regarding the need for retreatment. The volumetric data also provide insight into the magnitude of tissue augmentation achievable with each filler. Both HA and CaHA achieved clinically significant improvements, defined as meaningful restoration of midface projection and correction of age-related volume deficits. The mean volume gains of approximately 2.5-3.1 mL align with prior studies suggesting that moderate-volume injections (2-3 mL per side) can achieve a natural, aesthetically pleasing outcome without overcorrection. Importantly, these volumetric results correlate with subjective aesthetic improvements, reinforcing the reliability and clinical relevance of the measurements. Subgroup analyses from the included studies indicate that patient age, sex, and baseline midface deficit do not significantly alter volumetric outcomes, suggesting that both HA and CaHA can be effectively applied across diverse patient populations. Additionally, injection technique particularly deep supraperiosteal placement versus subcutaneous administration plays a critical role in achieving optimal volume retention. Studies consistently report that deeper placement enhances structural support, maximizes filler longevity, and minimizes surface irregularities.

Another important observation is the variability in volumetric retention among different HA formulations. Highly cross-linked HA generally maintains volume longer than low-cross-linked products, whereas CaHA exhibits a consistently durable profile regardless of minor formulation differences, owing to its collagen-stimulating properties. This distinction emphasizes the importance of considering filler rheology and tissue mechanics when planning treatment. The table also highlights the importance of integrating objective volumetric assessment with clinical judgment. While volumetric gain provides measurable data, patient satisfaction, natural appearance, and avoidance of overcorrection remain paramount in aesthetic practice. Objective metrics should guide clinical planning but must be interpreted within the context of overall aesthetic goals.

In conclusion, Table 3 demonstrates that both HA and CaHA are effective in restoring midface volume, with similar performance in the early month's post-injection. By 12 months, CaHA maintains significantly higher volumetric augmentation, supporting its use for patients seeking longer-lasting outcomes. These findings underscore the complementary roles of HA and CaHA in midface volumization, with HA suitable for immediate, reversible enhancement and CaHA offering durable structural correction. The data provide a quantitative foundation for evidence-

based treatment planning, patient counseling, and future comparative research in facial aesthetics.

Duration of Effect

CaHA exhibited superior durability. At 12 months, 78% of participants in CaHA groups maintained ≥75% of their initial volume augmentation, compared to 62% in HA groups. This trend was consistent across multiple studies, supporting CaHA's bio stimulatory advantage.

Table 4. Proportion of Participants Maintaining ≥75% Volume Retention

Filler	3 months	6 months	12 months
HA	92%	85%	62%
CaHA	94%	88%	78%

Table 4 provides a comparative overview of the proportion of participants who maintained at least 75% of their initial midface volumetric augmentation following treatment with hyaluronic acid (HA) and calcium hydroxylapatite (CaHA) at 3, 6, and 12 months. This metric serves as a critical indicator of long-term efficacy, durability, and the clinical relevance of dermal fillers in achieving sustained aesthetic results. At the 3-month follow-up, 92% of HA-treated participants and 94% of CaHA-treated participants retained ≥75% of the initial volume. These data suggest that both fillers deliver effective early volumetric correction, with minimal difference between the two groups. Early retention rates are important because they reflect not only the immediate filler effect but also patient satisfaction and confidence in the treatment. The near-universal retention at this stage demonstrates that both HA and CaHA reliably achieve the intended augmentation during the initial post-injection period.

By the 6-month interval, retention rates remained high for both fillers 85% for HA and 88% for CaHA. While there is a slight numerical advantage for CaHA, the difference is not statistically significant, indicating that both products maintain considerable volumetric persistence within the first half-year. This period is clinically meaningful because patients often assess the stability of results, and practitioners may use these early follow-ups to determine the need for touch-up or reinforcement injections. The consistency of retention across multiple studies further supports the reproducibility of these outcomes.

At 12 months, however, the difference between fillers becomes more pronounced. Only 62% of HA-treated participants retained ≥75% of the initial volume, whereas 78% of CaHA-treated participants maintained this threshold. This finding underscores the superior long-term durability of CaHA, likely attributable to its dual mechanism of action: immediate volume provision and gradual bio stimulatory effects leading to neocollagenesis. In contrast, HA is primarily resorbed over time, and while cross-linked formulations can extend longevity, the natural enzymatic degradation results in a gradual decline in volume. This long-term distinction is crucial for clinical decision-making, as it influences retreatment intervals, patient expectations, and overall satisfaction with the procedure. The data also highlight the impact of filler rheology and bio stimulatory potential on volume retention. CaHA's higher viscoelasticity contributes to its ability to support tissue architecture and resist deformation under dynamic facial movements. Additionally, the microsphere-mediated collagen stimulation provides structural reinforcement that maintains volumetric contours even as the gel carrier is absorbed. HA, while highly effective in the short term, lacks this intrinsic tissue-stimulating capacity, which explains the observed decline in long-term retention.

Subgroup considerations indicate that patient demographics such as age and sex do not substantially alter the proportion of participants maintaining ≥75% volume retention. This consistency supports the broad applicability of both HA and CaHA across a wide range of patients and demonstrates that the observed differences are largely due to filler properties rather than patient-specific factors. Furthermore, injection technique, including depth and distribution of filler, may influence retention. Deep supraperiosteal placement enhances long-term stability for both fillers, particularly for CaHA, reinforcing the importance of precise anatomical knowledge in achieving optimal outcomes.

The retention data also have important implications for treatment planning and economic considerations. Patients treated with CaHA may require fewer annual sessions due to its prolonged efficacy, potentially offsetting higher initial costs relative to HA. Conversely, HA may necessitate more frequent touch-ups to maintain comparable volumetric results, impacting both patient convenience and financial investment. These insights allow clinicians to provide individualized recommendations based on patient priorities, such as desired longevity, reversibility, and cost-effectiveness.

In summary, Table 4 demonstrates that while HA and CaHA are both highly effective in maintaining substantial midface volume in the early month's post-treatment, CaHA exhibits superior long-term retention at 12 months. The proportion of participants maintaining ≥75% of initial volume illustrates the durability advantage of CaHA,

supporting its preferential use in patients seeking prolonged aesthetic correction. These findings reinforce the complementary roles of HA and CaHA in clinical practice: HA offers predictable short-term enhancement with reversibility, whereas CaHA provides sustained volumization and structural support, making it suitable for patients prioritizing long-term outcomes. This analysis emphasizes the importance of integrating filler selection, injection technique, and patient expectations to optimize treatment planning and maximize clinical efficacy.

Safety and Adverse Events

Adverse events were generally mild and transient. The most common were swelling (HA 11%, CaHA 13%), erythema (HA 8%, CaHA 9%), and minor ecchymosis. Nodules were rare (HA 1%, CaHA 2%) and resolved with conservative management. No severe vascular complications or infections were reported.

Table 5. Incidence of Adverse Events

Adverse Event	HA (%)	CaHA (%)
Swelling	11	13
Erythema	8	9
Ecchymosis	3	4
Nodules	1	2
Infection	0	0

Table 5 summarizes the incidence of common adverse events associated with midface volumization using hyaluronic acid (HA) and calcium hydroxylapatite (CaHA). The table includes key complications such as swelling, erythema, ecchymosis, nodules, and infection, providing an evidence-based overview of safety profiles for both filler types. Understanding these outcomes is critical for clinicians to evaluate risk, inform patient counseling, and guide clinical decision-making in aesthetic practice.

The data demonstrate that swelling is the most frequently reported adverse event for both fillers, occurring in 11% of HA-treated participants and 13% of CaHA-treated participants. Swelling is typically mild to moderate, transient, and resolves within several days to weeks. The slightly higher incidence in CaHA may be attributed to its particulate nature and potential tissue-stimulating effect, which can induce localized edema during the early post-injection period. Importantly, most studies report that swelling did not necessitate medical intervention and did not compromise overall aesthetic outcomes.

Erythema was reported in 8% of HA cases and 9% of CaHA cases. This mild redness is generally self-limited, resulting from localized vascular irritation during needle insertion or minor inflammatory response to the filler material. Similar to swelling, erythema is transient and often resolves without intervention. Its occurrence underscores the importance of proper injection technique, atraumatic handling, and post-procedure care to minimize patient discomfort and optimize recovery. Ecchymosis, or bruising, was observed in 3% of HA participants and 4% of CaHA participants. Bruising is commonly related to inadvertent capillary injury during injection, and its low incidence indicates that both fillers are generally safe when administered by experienced clinicians. Strategies such as avoiding high-risk vascular areas, using appropriate needle or cannula techniques, and applying post-injection cold compresses can further reduce the likelihood of ecchymosis. Nodules were rare, reported in only 1% of HA cases and 2% of CaHA cases. Nodular formation is typically associated with superficial placement, overcorrection, or aggregation of filler particles. The slightly higher rate in CaHA is consistent with its particulate composition and bio stimulatory properties, which may occasionally provoke localized tissue reaction. However, most nodules resolved spontaneously or responded to conservative management. Notably, HA nodules can often be dissolved with hyaluronidase, providing an additional safety mechanism that is not available for CaHA, emphasizing the importance of informed patient selection and injection expertise.

Infection was not reported in any participants across the studies, highlighting that adherence to aseptic technique and standard clinical protocols effectively mitigates this risk. The absence of serious complications, such as vascular occlusion or granuloma formation, reinforces the safety profile of both HA and CaHA when administered by trained professionals.

Comparative analysis indicates that both HA and CaHA share similar safety profiles, with predominantly mild and transient adverse events. The minor differences observed, such as slightly higher swelling or nodules with CaHA, are clinically manageable and do not significantly impact patient outcomes or satisfaction. These findings align with previous literature, which consistently reports high safety and tolerability for both filler types in midface augmentation.

Furthermore, the table provides valuable insights for patient counseling. Clinicians can inform patients that while mild swelling, erythema, and bruising are possible, these events are typically temporary and self-limited. The slightly higher likelihood of nodules with CaHA should be discussed, particularly with patients prioritizing reversibility,

as HA provides an option for enzymatic correction in rare cases of adverse reactions. Transparency regarding potential side effects enhances patient trust and satisfaction, contributing to better overall treatment experience.

In conclusion, Table 5 demonstrates that both HA and CaHA are safe for midface volumization, with low incidences of mild and manageable adverse events. The safety profiles are comparable, with no serious or long-term complications reported, supporting their widespread use in clinical practice. Clinicians should focus on meticulous injection technique, patient selection, and post-procedure care to further minimize risks. These findings reinforce that safety considerations, while important, do not compromise the efficacy of either filler, allowing practitioners to select products based on desired aesthetic outcomes, durability, and patient-specific preferences. Overall, the data from Table 5 affirm the favorable risk-benefit profile of HA and CaHA in midface augmentation.

Subgroup Analysis by Age and Gender

Subgroup analyses revealed no significant differences in aesthetic outcomes between age groups (≤50 vs >50) or gender. Both fillers demonstrated similar efficacy, indicating broad applicability across diverse patient populations.

Table 6. GAIS Scores by Age Group (Mean ± SD)

Age Group	HA	CaHA
≤50	3.8 ± 0.4	3.9 ± 0.5
>50	3.6 ± 0.4	3.7 ± 0.4

Table 6 presents the mean Global Aesthetic Improvement Scale (GAIS) scores for hyaluronic acid (HA) and calcium hydroxylapatite (CaHA) stratified by age groups (≤50 years and >50 years). This analysis provides insights into the influence of patient age on perceived aesthetic improvement and treatment efficacy following midface volumization. Understanding age-specific outcomes is essential for tailoring clinical interventions, setting realistic expectations, and optimizing satisfaction across diverse patient populations.

The GAIS is a validated scale that combines clinician evaluation with patient-reported satisfaction to quantify aesthetic improvement, with higher scores indicating greater enhancement. In Table 6, HA-treated participants ≤50 years achieved a mean score of 3.8±0.4, while those >50 years had a slightly lower mean of 3.6±0.4. Similarly, CaHA-treated participants ≤50 years scored 3.9±0.5, with older participants >50 years scoring 3.7±0.4. Overall, both fillers demonstrate substantial improvement across all age groups, confirming their effectiveness in midface augmentation.

These findings suggest that patient age does not significantly diminish treatment outcomes. Younger patients (≤50 years) and older patients (>50 years) experienced comparable aesthetic enhancement, with only minimal differences in mean GAIS scores. The slightly higher scores in younger patients may reflect differences in baseline skin elasticity, soft tissue quality, and tissue responsiveness to filler material. Younger dermal tissue tends to exhibit greater recoil and volumetric support, potentially enhancing filler projection and natural contour restoration. Conversely, age-related changes, including dermal thinning, fat compartment atrophy, and skeletal remodeling, may slightly reduce immediate filler projection in older individuals; however, the differences observed in Table 6 are minor and clinically insignificant.

CaHA consistently showed marginally higher GAIS scores compared to HA across both age groups, indicating that its bio stimulatory properties contribute to perceived improvement regardless of patient age. The collagen-stimulating effect of CaHA not only augments volume but also enhances skin quality, firmness, and tissue resilience, which may be particularly beneficial in older patients who experience greater age-related tissue atrophy. This feature helps maintain aesthetic outcomes and may explain why CaHA scores remain relatively stable across age groups compared to HA.

The minimal impact of age on GAIS scores also emphasizes the versatility of HA and CaHA in clinical practice. Both fillers are suitable for a wide range of adult patients seeking midface volumization, without the need for age-based modification of injection strategy solely for efficacy reasons. However, clinicians should still consider age-related anatomical differences when planning injection depth, volume, and distribution. For instance, deeper placement may be warranted in older patients to achieve optimal structural support, while superficial layering may suffice in younger individuals with adequate soft tissue volume.

In addition to efficacy, patient-reported satisfaction is a critical component captured by GAIS scores. Across studies, both age groups reported high satisfaction, indicating that subjective perception of facial rejuvenation aligns with objective volumetric gains. This concordance suggests that both HA and CaHA effectively meet patient expectations in diverse age populations, enhancing overall treatment value.

It is also noteworthy that GAIS scores reflect not only filler performance but also the quality of injection technique, practitioner experience, and post-procedural care. Consistency in high scores across age groups implies that these factors were

well-controlled in the included studies, reinforcing the reliability of the results.

In conclusion, Table 6 demonstrates that both HA and CaHA produce significant aesthetic improvement regardless of age, with only minor differences observed between younger and older patients. CaHA shows slightly higher GAIS scores across all age groups, likely due to its collagen-stimulating and tissue-supporting properties. These findings highlight the broad applicability of both fillers, confirming their efficacy in achieving midface volumization across the adult age spectrum. Clinicians can confidently offer either filler to patients of varying ages, tailoring injection technique and volume to individual anatomical needs without concern for substantial age-related differences in perceived outcomes.

Comparative Cost-effectiveness

While not uniformly reported, some studies included an economic analysis, suggesting that CaHA's longer-lasting effects may reduce the frequency of repeat injections compared to HA, potentially offsetting higher upfront costs.

Table 7. Estimated Cost per Year of Maintenance ($USD)

Filler	Average Cost per Session	Frequency per Year	Total Annual Cost
HA	400	2	800
CaHA	450	1	450

The aggregated results indicate that both HA and CaHA are highly effective for midface volumization, achieving significant aesthetic improvement and volumetric gains. HA offers immediate and reversible enhancement, while CaHA demonstrates a more durable effect at 12 months, likely due to collagen stimulation. Safety profiles are comparable, with mostly transient adverse events. Cost-effectiveness analyses favor CaHA when long-term results are considered. Subgroup analyses suggest consistent efficacy across age and gender, supporting the broad applicability of both fillers [32-34].

Collectively, these findings support the conclusion that HA is ideal for patients prioritizing reversibility and short-term results, whereas CaHA is advantageous for durable structural correction and long-term tissue remodeling.

Table 7 presents a comparative assessment of the estimated annual cost of midface volumization maintenance using hyaluronic acid (HA) and calcium hydroxylapatite (CaHA). The table considers both the average cost per treatment session and the typical frequency of injections required to sustain optimal aesthetic outcomes, thereby providing a practical perspective on the economic implications of long-term filler therapy. Cost-effectiveness is a critical factor for both patients and clinicians, as it influences treatment planning, adherence to follow-up schedules, and overall satisfaction with aesthetic interventions.

According to the table, the average cost per session for HA is $400, with an expected frequency of two sessions per year, resulting in a total annual cost of $800. In contrast, CaHA has a slightly higher per-session cost of $450 but typically requires only one session per year due to its prolonged durability, yielding a total annual cost of $450. These data highlight an important economic consideration: although HA may have a lower upfront cost, the necessity for more frequent treatments increases the cumulative annual expenditure compared to CaHA. This analysis underscores the value of considering both short-term and long-term costs when counseling patients on filler selection.

The observed difference in annual cost can be directly linked to the pharmacological and physiological properties of the fillers. HA is primarily resorbed over time through enzymatic degradation, necessitating more frequent touch-ups to maintain consistent volume and aesthetic results. In contrast, CaHA's dual mechanism immediate volumization and bio stimulation of collagen ensures a more durable effect, reducing the frequency of maintenance injections. Consequently, while the initial investment in CaHA may be slightly higher per session, the extended longevity offers a lower long-term financial burden, making it a potentially more cost-effective option for patients seeking sustained midface augmentation.

Beyond direct financial considerations, cost-effectiveness also encompasses clinical outcomes, patient satisfaction, and convenience. Fewer injection sessions with CaHA not only reduce the overall cost but also decrease the cumulative risk of procedure-related adverse events, minimize recovery time, and improve patient convenience. These benefits are particularly meaningful for patients with limited availability, higher sensitivity to procedural discomfort, or those prioritizing long-term treatment efficiency [35-37].

The table also prompts consideration of individualized patient decision-making. For patients desiring immediate, reversible results, HA may remain the preferred option despite higher annual costs, particularly when patient preference or anatomical considerations favor its use. Conversely, patients prioritizing long-lasting volume restoration, structural support, and fewer interventions may find CaHA to be the superior choice from both clinical and economic perspectives. This highlights the importance of integrating cost-effectiveness data into comprehensive treatment planning, alongside efficacy, safety, and patient-specific goals [38-40].

Furthermore, Table 7 underscores the need to account for variability in pricing across geographic regions, clinical settings, and filler brands. Actual costs may differ depending on local market conditions, provider expertise, and the specific formulation used. Nevertheless, the relative trend observed higher per-session cost but lower annual expenditure for CaHA remains a consistent finding across multiple studies and aligns with broader economic analyses in aesthetic medicine.

From a health economics perspective, the long-term cost savings associated with CaHA may enhance patient adherence to maintenance schedules, potentially improving sustained clinical outcomes and overall satisfaction. Patients who perceive treatments as financially manageable are more likely to maintain regular follow-up visits, which further supports optimal aesthetic results and minimizes the risk of uneven or suboptimal volumization over time [41-43].

In conclusion, Table 7 demonstrates that while HA offers lower upfront session costs, the need for biannual treatments results in a higher annual expenditure compared to CaHA. CaHA's prolonged durability and reduced treatment frequency provide both economic and practical advantages, making it a cost-effective option for patients seeking long-term midface volumization. This analysis reinforces the importance of considering economic factors alongside clinical efficacy, safety, and patient preference when selecting dermal fillers. Integrating cost considerations into patient counseling ensures informed decision-making, aligns treatment plans with individual priorities, and supports sustainable aesthetic outcomes in clinical practice [44].

Discussion

This systematic review and meta-analysis demonstrate that both CaHA and HA provide effective midface volumization with favorable safety profiles. Early aesthetic outcomes up to 6 months' post-injection are comparable; however, CaHA may offer longer durability a finding consistent with its biostimulatory mechanism encouraging collagen production [45-47].

Clinicians should consider patient goals (e.g., longevity, reversibility), cost, and filler properties when selecting agents. HA is reversible via hyaluronidase, which is advantageous in managing complications. CaHA's longer effect and collagen stimulation may be preferable for patients seeking extended results.

Limitations: Variability in outcome measures and imaging techniques across studies. Larger standardized RCTs are required to confirm these findings. The seven tables presented in this study collectively provide a detailed, multidimensional evaluation of the efficacy, durability, safety, demographic applicability, and economic considerations of hyaluronic acid (HA) and calcium hydroxylapatite (CaHA) for midface volumization. By synthesizing data from study characteristics, aesthetic outcomes, volumetric measurements, long-term retention, adverse events, subgroup analyses, and cost implications, a comprehensive understanding of these widely used dermal fillers emerges. This integrated analysis enables evidence-based clinical decision-making and informs future research directions.

Table 1, outlined the characteristics of the included studies, highlighting a combination of randomized controlled trials (RCTs) and prospective cohort studies encompassing 1,245 participants with diverse demographic profiles. The inclusion of both study types ensures a balanced perspective, incorporating rigorous experimental evidence alongside real-world clinical observations. Sample sizes ranged from 80 to 200 participants, allowing for adequate statistical power in most analyses while capturing the variability inherent in clinical practice. The studies utilized both HA and CaHA, with follow-up durations spanning 3 to 24 months, thereby enabling both short-term and long-term assessment of filler performance. Injection volumes varied from 1.0 to 4.0 mL per midface region, reflecting patient-specific needs and emphasizing the importance of individualized treatment planning. Importantly, the studies incorporated validated outcome measures, including the Global Aesthetic Improvement Scale (GAIS), patient satisfaction surveys, and objective volumetric analyses, providing a multidimensional view of treatment efficacy [48-50].

Table 2, presented mean aesthetic improvement scores, demonstrating that both HA and CaHA produced substantial perceived improvement in midface contour across 3-, 6-, and 12-month follow-ups. While early outcomes (3-6 months) were largely equivalent between the fillers, CaHA maintained slightly higher scores at 12 months. This reflects its bio stimulatory properties, promoting collagen production and extracellular matrix remodeling, which enhance long-term aesthetic outcomes. Patient-reported satisfaction aligned closely with GAIS scores, underscoring that both fillers meet patient expectations in the short and long term. These findings highlight the complementary roles of HA and CaHA, with HA suitable for immediate, reversible enhancement and CaHA offering durable structural correction [51-53].

Table 3, provided objective volumetric data, revealing that both fillers achieved meaningful increases in midface volume. Initial gains were comparable at 3 and 6 months, with HA at 2.8±0.6 mL and CaHA at 2.9±0.5 mL at 6 months. By 12 months, CaHA maintained higher volumetric retention (3.1±0.5 mL) compared to HA (2.3±0.5mL), highlighting its superior durability. These objective measurements corroborate subjective aesthetic improvements and support the

notion that CaHA's collagen-stimulating effects contribute to long-term tissue support, whereas HA, though effective, undergoes gradual enzymatic resorption. Volumetric analyses provide critical quantitative evidence for planning retreatment intervals and predicting long-term outcomes [54].

Table 4, focused on the proportion of participants maintaining ≥75% of initial volume, a direct measure of filler longevity. Both fillers exhibited high early retention rates (3 months: HA 92%, CaHA 94%; 6 months: HA 85%, CaHA 88%), indicating effective initial correction. At 12 months, a notable divergence emerged: 62% of HA participants versus 78% of CaHA participants maintained this threshold. This reinforces the concept that CaHA provides more sustained volumetric effect, offering a practical advantage for patients seeking longer-lasting results and reducing the need for frequent touch-ups.

Table 5, analyzed adverse events, revealing that both fillers are generally safe and well-tolerated. Mild and transient events swelling, erythema, and ecchymosis were most common, occurring in similar frequencies for HA and CaHA. Nodules were rare (HA 1%, CaHA 2%) and manageable, while no infections or serious complications were reported. Safety profiles were largely comparable, affirming that both fillers can be used confidently in clinical practice. However, HA's reversibility via hyaluronidase provides an additional safety advantage in the rare case of adverse outcomes.

Table 6, examined GAIS scores by age group, demonstrating that patient age minimally influenced aesthetic outcomes. Younger (≤50 years) and older (>50 years) participants achieved comparable improvements with both fillers, although CaHA maintained slightly higher scores across age groups. These findings indicate that both HA and CaHA are versatile, applicable across adult populations, and effective regardless of age-related tissue changes, with CaHA offering additional benefits for patients with more pronounced age-related volume loss due to its bio stimulatory properties.

Table 7, evaluated estimated cost per year of maintenance, highlighting the economic implications of filler selection. HA required more frequent treatments (biannual), leading to a higher total annual cost ($800) compared to CaHA ($450), which generally requires only one session annually due to its prolonged durability. These findings underscore CaHA's potential cost-effectiveness, reducing both financial burden and patient inconvenience while maintaining superior long-term outcomes. Economic considerations, combined with efficacy and safety profiles, are essential for informed patient counseling and strategic treatment planning.

Synthesizing insights from all seven tables, several key conclusions emerge. First, both HA and CaHA provide significant aesthetic and volumetric improvement in midface augmentation, with high patient satisfaction and minimal adverse events. Second, CaHA consistently demonstrates superior durability, maintaining higher volumetric gains, aesthetic scores, and retention percentages at 12 months. Third, safety profiles are comparable, though HA offers the advantage of reversibility. Fourth, age does not significantly affect outcomes, supporting broad applicability. Finally, long-term cost analysis favors CaHA due to reduced injection frequency and sustained efficacy.

In summary, the integrated analysis of the seven tables provides robust evidence that both HA and CaHA are effective, safe, and clinically valuable for midface volumization. HA excels in immediate, reversible enhancement, while CaHA is superior for long-lasting volumetric correction, structural support, and economic efficiency. These findings offer practical guidance for clinicians in selecting appropriate fillers based on patient-specific goals, anatomical considerations, and long-term treatment planning, ultimately supporting optimized aesthetic outcomes and patient satisfaction [55].

Conclusion

Both calcium hydroxylapatite and hyaluronic acid are effective, safe options for midface volumization. While short-term aesthetic results are similar, CaHA may confer a more durable response. Future research should prioritize standardized endpoints and longer follow-up.

This systematic review and meta-analysis provides a comprehensive evaluation of the efficacy, durability, safety, and economic implications of hyaluronic acid (HA) and calcium hydroxylapatite (CaHA) in midface volumization. By synthesizing data from seven key tables encompassing study characteristics, aesthetic outcomes, volumetric measurements, long-term retention, adverse events, age-specific responses, and cost analysis, the findings offer robust evidence to guide clinical decision-making and optimize patient outcomes.

Both HA and CaHA demonstrated significant efficacy in restoring midface volume and improving facial aesthetics. Objective volumetric assessments and subjective aesthetic scores confirmed meaningful improvement relative to baseline across all included studies. Short-term results (3–6 months) were largely equivalent between the two fillers, reflecting effective immediate augmentation and high patient satisfaction. These findings affirm that both HA and CaHA are reliable options for patients seeking non-surgical midface enhancement.

Long-term outcomes reveal a clear distinction between the two filler types. At 12 months, CaHA consistently maintained higher volumetric gains, aesthetic improvement scores, and proportions of participants retaining ≥75% of initial volume compared to HA. This durability is attributed to CaHA's dual mechanism: immediate physical

volume from its gel matrix and progressive bio stimulatory effects that stimulate collagen production and extracellular matrix remodeling. In contrast, HA, while highly effective initially, is gradually resorbed, resulting in modest reductions in volumetric and aesthetic outcomes over time. Clinically, these differences inform treatment planning: HA may be favored for patients prioritizing reversibility and short-term results, whereas CaHA is ideal for those seeking sustained volume, structural support, and longer-lasting enhancement.

Safety profiles for both HA and CaHA were favorable, with mostly mild, transient, and manageable adverse events, including swelling, erythema, and ecchymosis. Nodules were rare, and no infections or severe complications were reported. HA offers an additional safety advantage due to its enzymatic reversibility with hyaluronidase, which can rapidly correct any undesired outcomes. Nevertheless, the overall risk-benefit profile is highly favorable for both fillers, supporting their widespread clinical use.

Age did not significantly influence outcomes, indicating that both HA and CaHA are effective across adult populations, including older patients with age-related midface volume loss. CaHA's collagen-stimulating properties may confer additional benefits in older individuals by enhancing tissue quality and providing structural support, thereby maintaining aesthetic improvement even in the context of reduced skin elasticity and soft tissue atrophy. This versatility underscores the broad applicability of these fillers in diverse patient populations.

Economic considerations further differentiate these fillers. Although HA has a lower cost per individual session, the need for more frequent injections results in higher cumulative annual costs compared to CaHA. CaHA's prolonged durability allows for fewer annual treatments, offering both financial and practical advantages for patients seeking long-term results. Integrating cost-effectiveness into treatment planning ensures informed decision-making, improved adherence to maintenance schedules, and sustained patient satisfaction.

In conclusion, both HA and CaHA are effective, safe, and reliable for midface volumization, providing immediate and meaningful aesthetic enhancement. HA is best suited for patients seeking reversible, short-term results, while CaHA offers superior long-term durability, tissue support, and cost-effectiveness. Clinicians should consider patient-specific goals, anatomical characteristics, age, and financial factors when selecting the optimal filler. The evidence synthesized in this review reinforces the complementary roles of HA and CaHA in facial aesthetics and highlights the importance of individualized, evidence-based treatment planning to achieve optimal clinical outcomes and long-term patient satisfaction.

Acknowledgments

All authors of this article confirm the authenticity of the manuscript.

Conflicts of interest

The authors declare that they have no competing interests.

Disclosure Statement

No potential conflict of interest reported by the authors.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Authors' Contributions

All authors contributed to data analysis, drafting, and revising of the paper and agreed to be responsible for all the aspects of this work.

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