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Biological Supplementation for Facial Fat Graft Retention and Skin Rejuvenation: A Systematic Review

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Abstract

Autologous fat grafting is widely used to restore facial volume in aesthetic and reconstructive surgery, but unpredictable graft retention remains a major limitation. This systematic review assessed whether supplementation with stromal vascular fraction (SVF), adipose-derived stromal/stem cells (ADSCs), or platelet-rich plasma (PRP) improves graft retention or skin quality. PubMed was searched for prospective comparative studies published between January 2015 and April 2026. Nine studies involving 443 participants met the inclusion criteria; eight used randomized allocation. Six studies, including five randomized comparisons, reported significantly better objective retention outcomes with SVF- or ADSC-enriched fat than with conventional grafting, with follow-up of up to 12 months. Evidence for PRP was mixed: one nonrandomized study favored PRP, whereas two randomized comparisons found no significant improvement in the volumetric or contour outcomes assessed. One randomized trial reported faster postoperative recovery with PRP. Adding SVF to PRP-supplemented grafting did not show a clear additional benefit. Differences in interventions and outcome measures precluded meta-analysis. Cellular enrichment may improve facial fat graft retention, but the optimal product, preparation method, dose, and clinical indication remain uncertain.

Categories: Plastic Surgery, Dermatology
Keywords: adipose-derived stem cells, autologous fat transfer, facial rejuvenation, fat graft enrichment, fat graft retention, lipofilling, platelet-rich plasma, skin quality, stromal vascular fraction

Introduction And Background

Autologous fat grafting has become a widely used option for restoring facial soft-tissue volume in both reconstructive and aesthetic surgery [1]. Compared with synthetic fillers, such as hyaluronic acid and calcium hydroxyapatite, autologous fat is readily available, biocompatible, and minimally immunogenic; it can be shaped to correct age-related volume loss or reconstructive defects and has a generally low reported complication rate in facial applications [2-4].

Despite these advantages, graft retention remains unpredictable. Groen et al. reported retention ranging from 13% to 68% after a mean follow-up of 12.2 months [2], while other reviews have reported values of approximately 20% to 80% [4,5]. This variability likely reflects differences in harvesting, processing, injection technique, recipient anatomy, follow-up, and outcome measurement [1,2,4,5]. After transplantation, grafted fat initially depends on diffusion from the recipient bed until revascularization occurs [1,6]. Two complementary mechanisms have been proposed to explain graft retention: survival of transplanted adipocytes and replacement of adipocytes lost during graft remodeling. Experimental work suggests that peripheral adipocytes may survive, while adipocytes in more ischemic regions die and can be replaced by new adipocytes derived from adipose-derived stromal/stem cells (ADSCs); severe ischemia may instead lead to necrosis [7]. Mechanical injury during harvesting or injection may further compromise graft viability [1,6].

Biological products derived from adipose tissue or blood have therefore been investigated as strategies to improve graft retention. Cell-assisted lipotransfer supplements a fat graft with an adipose-derived cellular product, such as stromal vascular fraction (SVF) or culture-expanded ADSCs [5,8]. Zuk et al. demonstrated that adipose tissue contains multipotent stromal cells with characteristics similar to those of bone marrow-derived stromal cells [9]. ADSCs can differentiate into several lineages and have angiogenic, immunomodulatory, and paracrine properties that may support tissue exposed to hypoxia and ischemia [5,8,9]. SVF is a heterogeneous cell population containing ADSCs, endothelial cells or progenitors, fibroblasts, pericytes, and immune cells [10]. Enrichment with SVF or ADSCs could therefore support revascularization and graft survival under hypoxic conditions.

Platelet-rich plasma (PRP) represents an alternative biological strategy. It is an autologous plasma fraction with a platelet concentration above baseline, usually obtained by centrifugation [11]. Platelets release growth factors involved in tissue repair, including platelet-derived growth factor, insulin-like growth factor, vascular endothelial growth factor, and transforming growth factor beta [12]. PRP has therefore been proposed to improve fat graft retention and skin quality by promoting angiogenesis, collagen production, and tissue repair [12,13]. However, the relative effectiveness of SVF, ADSCs, and PRP and the value of combining them remain incompletely defined in facial lipofilling.

This systematic review examines prospective comparative evidence on facial lipofilling supplemented with SVF, ADSCs, PRP, or combinations of these products. Its primary objective is to compare graft volume retention with that achieved using conventional fat grafting or an appropriate placebo control. Secondary objectives are to evaluate facial skin quality, patient-reported outcomes, recovery, and adverse events, and to identify which biological strategies have demonstrated benefit and which protocol features require further study.

Review

Materials and methods

The design and reporting of this systematic review were guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement [14]. No review protocol was registered or published.

Eligibility criteria were defined using the PICOTS framework: Population, Intervention, Comparison, Outcomes, Time, and Study Setting. Eligible participants were adults aged 18 years or older undergoing autologous facial fat grafting for aesthetic or reconstructive volume restoration or rejuvenation. Interventions consisted of fat grafts supplemented with cellular or tissue SVF, culture-expanded ADSCs, PRP, or combinations of these products. Eligible comparators were conventional autologous fat grafting, saline placebo, or the same background lipofilling regimen without the additional biological supplement.

The primary outcome was quantitative graft volume retention assessed by three-dimensional surface imaging, computed tomography (CT), magnetic resonance imaging (MRI), or ultrasound. Secondary outcomes included skin elasticity, transepidermal water loss, wrinkles, texture, other imaging-based skin features, histologic findings, patient satisfaction, postoperative recovery, and treatment-related adverse events. A minimum postoperative follow-up of six weeks was required.

Eligible studies were prospective comparative clinical investigations, including randomized parallel-group trials, randomized split-face or split-treatment studies, and prospective nonrandomized comparisons. Studies were required to report primary data, include an eligible comparator, and provide a quantitative graft-retention or facial skin-quality outcome. Only peer-reviewed, English-language studies published from January 1, 2015, through April 30, 2026, were considered. The 2015 cutoff was selected to focus on contemporary fat-processing, cellular-isolation, and volumetric-assessment protocols.

Retrospective or uncontrolled studies, case reports, case series, animal or laboratory investigations, retracted publications, and studies without an eligible comparator or quantitative outcome were excluded. Studies combining facial and nonfacial populations were excluded when facial results could not be extracted separately. Studies evaluating stand-alone SVF, nanofat, or SVF gel rather than supplementation of a fat graft were also excluded, as were studies focused primarily on acne scars, wounds, or nonfacial anatomical sites.

A systematic literature search was conducted in MEDLINE through PubMed on April 30, 2026. The complete search strategy is presented in Table *1*. Results were restricted to English-language reports published from January 1, 2015, through April 30, 2026. The review was initially designed within a postgraduate project in aesthetic and anti-aging medicine using a predefined PubMed-based search strategy. This framework was retained during manuscript development to preserve consistency with the original study design. PubMed was selected because it provides broad coverage of peer-reviewed biomedical and surgical literature relevant to facial fat grafting and biological supplementation.

Search component	Search terms
Fat grafting	fat OR lipotransfer OR lipofilling OR lipografts
Facial context	face OR facial
Clinical context	aesthetic OR aging OR rejuvenation
Biological supplementation	stromal vascular fraction OR SVF OR cell assisted OR platelet rich plasma OR PRP

TABLE 1: PubMed search strategy.

Terms within each search component were combined using the Boolean operator OR, and the four search components were combined using AND.

Records were screened sequentially by title, abstract, and full text according to the prespecified eligibility criteria. Potentially relevant or ambiguous records were retained for assessment at the next stage, and studies were included only after confirmation that all eligibility criteria had been met.

Data from included studies were entered into a structured table covering study design, indication and population, sample size and completion, intervention and comparator, processing protocol, duration of follow-up, primary and secondary outcomes, quantitative results, patient-reported outcomes, adverse events, and study limitations. Numerical findings were checked against the original article text and tables by the review team.

Because the included studies differed substantially in biological interventions, anatomical sites, imaging methods, follow-up periods, and reported outcomes, the findings were synthesized qualitatively, and no meta-analysis was performed.

Results

Study Selection and Evidence Profile

The PubMed search retrieved 137 records. After title screening, 72 records underwent abstract assessment, and 22 reports were assessed in full text. Nine studies met all eligibility criteria and were included in the qualitative synthesis. The selection process is summarized in Figure *1*.

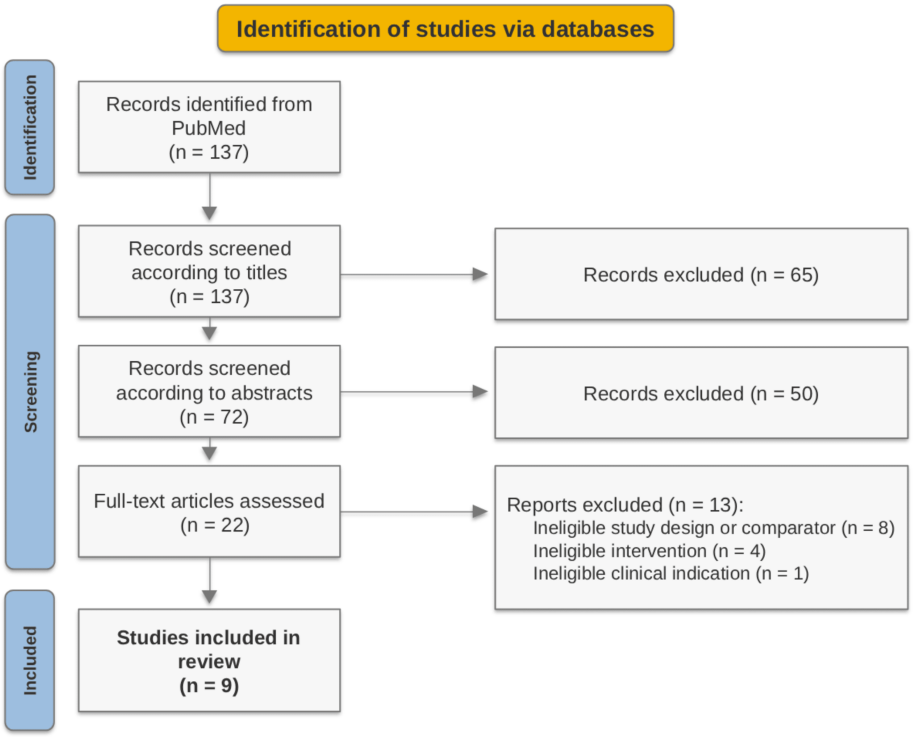


FIGURE 1: PRISMA flow diagram summarizing the study-selection process.

The nine included studies enrolled or randomized 443 participants, of whom 432 completed follow-up or were included in the final analyses [15-23]. Sample sizes ranged from 10 to 236. Eight studies used randomized parallel-group or split-face/split-treatment allocation, while one was a prospective nonrandomized comparison. Follow-up ranged from 24 weeks to 12 months. Indications included cosmetic facial rejuvenation, age-related temple or midface volume loss, post-traumatic or post-surgical defects, Parry-Romberg syndrome, and localized scleroderma.

Seven studies evaluated an SVF-containing strategy, three directly compared PRP with conventional or saline-supplemented fat, two included combined SVF and PRP supplementation, and one evaluated culture-expanded ADSCs; these categories overlap. Graft retention was assessed using three-dimensional surface imaging, CT, MRI, or ultrasound. Additional objective methods included cutometry, transepidermal water-loss measurement, and VISIA skin analysis. Subjective outcomes included blinded surgeon ratings, patient satisfaction scales, and FACE-Q. Study characteristics and principal findings are summarized in Table *2*.

Author	Year	n	Study Design	Outcome	Results
Sasaki [15]	2015	236	Prospective nonrandomized comparison during concurrent facelift surgery. Conventional fat (n = 92), fat plus PRP (n = 106), fat plus SVF (n = 9), or fat plus SVF and PRP (n = 29).	Vectra 3D surface-volume change through 12 months; blinded aesthetic assessment.	All supplemented groups showed greater 3D surface-volume retention than conventional fat at 12 months (P < 0.01). PRP and SVF were similar, and the combination added no further benefit. The large prospective cohort provides supportive evidence, although treatment was patient selected during concurrent facelift surgery.
Gontijo-de-Amorim et al. [16]	2017	30	Randomized parallel-group study. Conventional washed fat (n = 15) versus washed fat supplemented with a centrifugation-derived SVF-containing pellet (n	12-month CT volume loss in a randomly selected subset of five participants per group; blinded surgeon ratings;	CT subset: 9.6% volume loss with the SVF-containing pellet versus 24.0% with control (P = 0.013). Blinded surgeons assigned a mean 82.5% of ratings as excellent in the enriched group versus 47.6% in the control group; no major complication was reported.

			= 15).	adverse events.	
Willemsen et al. [17]	2018	32; 25 completed	Double-blind, placebo-controlled RCT. Fat plus PRP (13 completed) versus fat plus saline (12 completed).	12-month Cutometer skin elasticity, Merz nasolabial-fold grade, recovery, satisfaction, and adverse events.	PRP did not improve elasticity, satisfaction, or nasolabial-fold grade, but significantly shortened return to work/social activity: 9.1 versus 15.4 days with camouflage (P = 0.0101) and 14.9 versus 20.6 days without camouflage (P = 0.0112). Direct 3D volumetry was unavailable.
Sasaki [18]	2019	10	Randomized split-treatment study in 10 women. Fat plus PRP versus fat plus saline in opposing midfaces; with or without concurrent facelift surgery.	3D Vectra volume, VISIA/Cortex skin measures, blinded ratings, and adverse events at 3, 6, and 12 months.	3D volume changes were numerically greater with PRP at 3, 6, and 12 months, although between-side differences were not statistically significant. Skin measures did not differ, and no adverse event was reported.
Yin et al. [19]	2020	50	Randomized controlled trial. Fat plus cellular SVF (25) versus conventional fat (25). Healthy women aged 20–55 years.	6-month whole-face 3D volume retention and VISIA therapeutic-effect measures.	Retention was 77.6% versus 56.2% (P < 0.001). VISIA therapeutic-effect values for wrinkles and texture favored SVF; other measured skin domains did not differ.
van Dongen et al. [20]	2021	28; 25 completed	Double-blind, placebo-controlled RCT. All participants received PRP-supplemented lipofilling plus tissue SVF or saline.	12-month elasticity, TEWL, VISIA, FACE-Q, recovery, and complications.	Adding tissue SVF to PRP-supplemented lipofilling did not improve elasticity, TEWL, VISIA features, overall FACE-Q outcomes, or recovery. This trial provides evidence against an incremental benefit from the combined protocol.
Wang et al. [21]	2021	18	Randomized pilot trial. Conventional fat, fat plus SVF, or fat plus expanded ADSCs (six participants per group).	6-month MRI volume retention; blinded photographic ratings; adverse events.	Retention was 21.86%, 31.75%, and 49.83%; SVF exceeded control (P = 0.0346), ADSCs exceeded SVF (P = 0.0004), and ADSCs exceeded control (P < 0.0001).
Roshdy et al. [22]	2022	15	Single-center, double-blind randomized split-face trial in 15 otherwise healthy middle-aged women. Enzymatically prepared SVF-enriched temple fat versus conventional fat.	Temple Volume Scale, ultrasound biomicroscopy, satisfaction, and adverse effects at 1 week, 3 months, and 6 months.	At 6 months, the volume-deficit score was lower (0.5 versus 1.1, P = 0.0001) and hypodermal augmentation was greater (70.92% versus 18.93%, P = 0.001) with SVF; satisfaction and temporary sequelae were similar between sides.
Wufuer et al. [23]	2024	24; 23 analyzed	Blinded multicenter RCT. SVF-enriched fat (11 analyzed) versus conventional fat (12 analyzed).	MRI retention at 6 and 24 weeks; surgeon and patient ratings; safety.	MRI retention favored SVF at 6 weeks (74.50% versus 66.55%, P < 0.0255) and 24 weeks (71.27% versus 61.98%, P < 0.0120). Forehead retention favored SVF at both time points and cheek retention at 24 weeks; temple differences were not significant. Surgeon scores favored SVF at 24 weeks, patient scores did not differ, and no microbial growth or fat graft-related complication was reported.

TABLE 2: Characteristics and principal findings of the prospective comparative studies included in the systematic review.

ADSCs, adipose-derived stromal/stem cells; CT, computed tomography; MRI, magnetic resonance imaging; PRP, platelet-rich plasma; RCT, randomized controlled trial; SVF, stromal vascular fraction; TEWL, transepidermal water loss; 3D, three-dimensional

Individual Study Findings

In the largest study, Sasaki prospectively followed 236 patients undergoing a limited facelift procedure with concurrent anterior-midface fat grafting; patients selected conventional fat (n = 92), fat plus PRP (n = 106), fat plus SVF (n = 9), or fat plus SVF and PRP (n = 29) [15]. Vectra three-dimensional surface-volume changes were assessed through 12 months. At 12 months, all three supplemented groups showed significantly greater retention than the conventional-fat group ($P < 0.01$). PRP and SVF performed similarly, and the combined intervention was not superior to either supplement alone.

Gontijo-de-Amorim et al. randomized 30 participants with Parry-Romberg syndrome, post-traumatic defects, or post-surgical facial volume loss to conventional washed fat or washed fat supplemented with a centrifugation-derived SVF-containing pellet [16]. Quantitative CT was performed at 12 months in a randomly selected subset of five participants per group. Mean volume loss was 9.6% with the SVF-containing pellet and 24.0% with conventional fat ($P = 0.013$). Blinded surgeon ratings more frequently classified outcomes as excellent in the enriched group. No major complications were reported.

Willemsen et al. conducted a double-blind, placebo-controlled randomized trial in 32 healthy women undergoing aesthetic facial lipofilling; 25 completed follow-up, with 13 receiving fat plus PRP and 12 receiving fat plus saline [17]. PRP did not improve the primary endpoint of skin elasticity or the secondary outcomes of patient satisfaction and Merz nasolabial-fold grade at 12 months. Three-dimensional volumetry was abandoned because of inconsistent and irreproducible measurements, so the study did not provide a direct measure of graft volume retention. Recovery was shorter with PRP: return to work or social activity occurred after 9.1 versus 15.4 days when camouflage was used ($P = 0.0101$) and after 14.9 versus 20.6 days without camouflage ($P = 0.0112$).

Sasaki subsequently conducted a randomized split-treatment study in 10 women with age-related midface and hand changes; all participants completed one year of follow-up [18]. Each participant received fat plus PRP on one randomly assigned side and fat plus saline on the contralateral side, with matched facial and hand treatments and with or without concurrent facelift surgery. Facial outcomes included Vectra three-dimensional volume change, VISIA and Cortex skin measures, blinded aesthetic ratings, and adverse events at three, six, and 12 months. PRP produced numerically greater facial volume change than saline, but the between-side difference was not statistically significant. Skin measures also did not differ, and no adverse events were reported.

Yin et al. randomized 50 healthy women aged 20-55 years, all of whom completed follow-up, to SVF-enriched or conventional fat grafting and assessed whole-face volume by three-dimensional imaging and skin features with VISIA [19]. At six months, mean volume retention was 77.6% ± 11.6% with SVF and 56.2% ± 9.5% with conventional fat ($P < 0.001$). The reported VISIA therapeutic-effect values favored SVF for wrinkles (19.3 ± 6.6 versus 10.9 ± 5.5, $P < 0.001$) and texture (15.8 ± 7.0 versus 10.3 ± 5.0, $P = 0.003$). Spots, pores, ultraviolet spots, brown spots, red areas, and porphyrins did not differ significantly between groups. Most participants in both groups were satisfied, and no major complications were reported.

van Dongen et al. enrolled 28 healthy women in a double-blind, placebo-controlled randomized trial, of whom 25 completed follow-up [20]. All participants received PRP-supplemented facial lipofilling and were allocated to receive additional mechanically isolated tissue SVF or saline. Tissue SVF did not improve the primary outcomes of skin elasticity or transepidermal water loss at one year, and VISIA skin features did not differ between groups. No overall benefit was demonstrated in FACE-Q outcomes or recovery. At 12 months, satisfaction with overall facial appearance improved only in the control group.

Wang et al. randomized 18 participants with localized scleroderma, including 11 women and seven men, equally to conventional fat, SVF-enriched fat, or fat enriched with ex vivo expanded autologous ADSCs; all completed six months of follow-up [21]. MRI-assessed volume retention at six months was 21.86% ± 1.68% with conventional fat, 31.75% ± 1.73% with SVF, and 49.83% ± 3.61% with expanded ADSCs. SVF exceeded conventional fat ($P = 0.0346$), while expanded ADSCs exceeded both SVF ($P = 0.0004$) and conventional fat ($P < 0.0001$).

Roshdy et al. conducted a single-center, double-blind randomized split-face trial in 15 otherwise healthy middle-aged women undergoing bilateral temple augmentation with enzymatically prepared SVF-enriched fat on one side and conventional fat on the other [22]. Temple Volume Scale scores, ultrasound biomicroscopy, satisfaction, and adverse effects were assessed blindly at one week, three months, and six months. At six months, the SVF-enriched side had a lower Temple Volume Scale score, indicating less volume deficit (0.5 ± 0.5 versus 1.1 ± 0.7, $P = 0.0001$), and greater hypodermal augmentation on ultrasound (70.92% ± 58.09% versus 18.93% ± 19.33%, $P = 0.001$). Patient satisfaction was similar between sides, and temporary sequelae such as edema, ecchymosis, and lumping were comparable.

Wufuer et al. conducted a blinded multicenter randomized controlled trial; the full text reports that 24 participants were randomized, with 23 included in the final analyses: 11 receiving SVF-enriched fat and 12 receiving conventional fat [23]. Overall MRI-assessed graft retention favored SVF at six weeks (74.50% ± 9.99% versus 66.55% ± 13.77%, $P < 0.0255$) and 24 weeks (71.27% ± 10.43% versus 61.98% ± 13.46%, $P < 0.0120$). Regional analyses favored SVF in the forehead at both time points and in the cheeks at 24 weeks,

while temple retention did not differ significantly. Surgeon-assigned aesthetic scores favored SVF at 24 weeks (P = 0.030), whereas patient-assigned scores did not differ. No bacterial growth was detected in SVF cultures, and no fat graft-related complications were reported during follow-up.

Cross-Study Synthesis

Six studies, including five randomized comparisons, reported significantly better objective retention outcomes with SVF- or ADSC-enriched fat than with conventional fat [15,16,19,21-23]. Where comparable percentage measures were available, absolute between-group differences ranged from approximately eight to 28 percentage points. Findings based on reduced volume loss on CT and greater hypodermal preservation on ultrasound further supported this retention advantage [16,19,21-23]. The direction of effect was consistent across cellular products, facial regions, clinical indications, and measurement methods. However, heterogeneity precluded calculation of a pooled effect size or identification of a standardized protocol.

Skin-quality and perioperative outcomes showed more selective benefits. Yin et al. reported significantly greater improvement in wrinkles and texture with SVF enrichment [19], while Willemsen et al. demonstrated significantly faster postoperative recovery with PRP [17]. Other randomized comparisons did not demonstrate broad incremental benefits in elasticity, VISIA domains, or contour outcomes from PRP or from adding tissue SVF to PRP-supplemented lipofilling [17,18,20]. The most consistent evidence therefore concerned graft retention, although individual adjuncts produced benefits in specific secondary outcome domains.

Reported adverse events were generally transient and included edema, ecchymosis, firmness, contour irregularity, and lumping [15-23]. No included study reported a severe treatment-related complication, and Wufuer et al. reported neither microbial growth in SVF cultures nor fat graft-related complications [23]. However, the sample sizes and duration of follow-up were insufficient to exclude uncommon or delayed adverse events.

Discussion

Cellular Enrichment and Clinical Relevance

Cellular enrichment produced the most consistent efficacy signal in this review. Six of the nine prospective comparative studies, including five randomized comparisons, reported significantly better objective retention outcomes with SVF- or expanded ADSC-enriched fat than with conventional fat [15,16,19,21-23]. Benefits were demonstrated using CT, MRI, three-dimensional surface imaging, and ultrasound across both aesthetic and reconstructive populations. The consistency of these findings supports a reproducible retention advantage, although its magnitude appears to depend on the cellular product and treatment protocol.

The observed differences were also clinically appreciable in several studies. Gontijo-de-Amorim et al. reported volume loss of 9.6% with SVF enrichment versus 24.0% with conventional fat at 12 months [16]. Yin et al. found a 21.4-percentage-point advantage in whole-face retention at six months [19], while Wufuer et al. reported a 9.29-percentage-point advantage on MRI at 24 weeks [23]. Roshdy et al. also demonstrated greater hypodermal preservation and a lower temple volume-deficit score with SVF in a randomized within-participant comparison [22]. Together, these findings indicate measurable preservation of grafted facial volume across different clinical settings.

The Wang trial is particularly informative because it directly compared conventional fat, point-of-care SVF enrichment, and culture-expanded ADSCs within a randomized design [21]. Expanded ADSCs produced the highest six-month retention, followed by SVF and conventional fat, with blinded clinical assessments showing the same ordering [21]. These findings suggest that biological supplementation should not be regarded as a uniform intervention and that the cellular product and dose may materially influence the outcome. The large prospective Sasaki cohort extended the favorable retention signal to 236 patients and 12 months, with all supplemented groups outperforming conventional fat, although treatment selection was not randomized [15].

The clinical findings are biologically plausible. SVF contains ADSCs, endothelial cells or progenitors, fibroblasts, pericytes, and immune cells [10]. ADSCs may support graft survival through angiogenic and cytoprotective paracrine signaling, modulation of inflammation, differentiation, and promotion of revascularization [8-10,24]. The repeated retention advantage observed across the included studies is compatible with these mechanisms, although the clinical evidence cannot determine which cellular components or pathways contribute most to the effect.

Variation in SVF preparation is likely to influence treatment performance and remains an important target for optimization. Mechanical, centrifugation-based, and enzymatic isolation methods produce cellular products that differ in composition, viable-cell yield, and extracellular-matrix content [10,20,24]. The included studies also varied in supplement-to-fat ratios, processing times, and delivery protocols [15,16,19-

23]. Such differences may contribute to the variation in effect magnitude and support standardized reporting of total nucleated-cell and viable-cell counts, cellular phenotype, supplement-to-fat ratio, interval from harvest to injection, and sterility controls.

PRP, Combination Strategies, and Skin Outcomes

PRP findings were heterogeneous. The largest prospective comparison reported better retention with PRP at 12 months [15], while the randomized split-treatment study by Sasaki showed a consistent but nonsignificant numerical trend in the same direction [18]. Willemsen et al. found no improvement in skin elasticity or facial contour but demonstrated a significant reduction in postoperative recovery time [17]. Overall, the randomized evidence did not establish a reproducible benefit of PRP for long-term retention, contour, or skin elasticity [17,18]. PRP may therefore offer perioperative or protocol-specific advantages, but its effect on graft retention is less consistent than that observed with cellular enrichment.

Interpretation is further complicated by substantial variation among PRP products. Preparations differ in platelet dose, leukocyte and erythrocyte content, fibrin architecture, activation method, and centrifugation protocol, while patient-related and pre-analytical factors may also influence biological quality [25,26]. This heterogeneity may contribute to protocol-dependent effects and limits extrapolation between studies. Future facial lipofilling trials should therefore characterize the PRP product and report platelet dose, leukocyte and erythrocyte content, activation and centrifugation methods, PRP-to-fat ratio, and delivery protocol [15,17,18,25,26].

Combination strategies yielded a separate clinically relevant finding: no additive benefit was demonstrated. In the Sasaki cohort, combined SVF and PRP supplementation was not superior to either product alone [15]. Similarly, in the van Dongen trial, adding tissue SVF to PRP-supplemented lipofilling did not improve skin elasticity, transepidermal water loss, VISIA features, FACE-Q outcomes, or recovery [20]. These findings do not negate the potential value of either product when used separately, but they indicate that biological synergy should not be assumed and that additional processing complexity and cost require evidence of incremental benefit.

Beyond volume retention, biological supplementation may also influence skin quality, although the observed benefits were selective. Yin et al. demonstrated significantly greater improvement in wrinkles and texture with SVF enrichment [19]. By contrast, Willemsen et al. and van Dongen et al. did not identify broad incremental improvements in objective elasticity or other skin-quality measures from PRP or tissue SVF, respectively [17,20]. The evidence therefore supports a stronger conclusion for graft retention than for generalized skin rejuvenation, while preserving a credible signal in specific skin domains.

Objective retention and patient-perceived benefit did not always move in parallel. Roshdy et al. and Wufuer et al. demonstrated objective advantages for SVF without significant between-group differences in patient satisfaction [22,23]. This is not necessarily contradictory: regional volume differences may be detectable by imaging yet remain less perceptible to patients, while satisfaction reflects the overall procedure rather than graft survival alone. Future trials should therefore include both objective volumetric assessment and validated patient-reported outcomes, as these measures address complementary aspects of clinical benefit.

Clinical Applicability, Safety, and Research Priorities

From a clinical perspective, the available evidence supports cellular enrichment as a promising strategy, particularly when durable retention is difficult to achieve, or repeat procedures would impose a substantial burden [16,19,21-23]. No single preparation can yet be considered universally superior, but the evidence has progressed beyond biological plausibility to repeated prospective comparative demonstration of improved objective retention. Clinical use should therefore be considered in relation to the indication, processing capability, cost, and local regulatory requirements, while recognizing that the most consistent efficacy signal concerns SVF- or ADSC-based enrichment.

The short-term safety profile was favorable. Among the 432 participants who completed follow-up or were included in the final analyses, no study reported a severe treatment-related complication [15-23]. Minor edema, bruising, firmness, contour irregularity, and lumping were generally transient, while the multicenter Wufuer trial reported neither microbial contamination of SVF cultures nor fat graft-related complications [23]. Larger cohorts and longer surveillance are still required to detect uncommon or delayed events, particularly with culture-expanded cellular products, but the available evidence supports procedural tolerability over six to 12 months.

This review has several limitations. The literature search was restricted to PubMed, and no complementary searches were conducted in other databases. Reliance on a single database reduced search comprehensiveness and may have resulted in the omission of eligible studies indexed exclusively elsewhere. The findings should therefore be interpreted as a synthesis of the prospective comparative evidence identified through PubMed rather than as an exhaustive representation of all potentially available evidence. The search was restricted to English-language reports and to studies published from 2015 onward, so eligible

evidence may have been missed. The included studies also differed in biological products, anatomical sites, clinical indications, and outcome measures, while randomized samples were often small. Follow-up did not exceed 12 months, and the largest study used patient-selected treatment during concurrent facelift surgery [15]. These factors precluded meta-analysis and prevented identification of a single optimal protocol, although the direction of the objective retention findings was consistent.

The inclusion of both aesthetic and reconstructive populations broadens the clinical scope of the review but limits direct interchangeability between settings. Benefits were observed in healthy patients seeking rejuvenation, patients with temple or midface volume loss, and patients with Parry-Romberg syndrome, post-traumatic defects, or localized scleroderma [16,19,21-23]. This suggests that cellular enrichment may be effective across different recipient environments, but future trials should stratify healthy, scarred, and sclerotic tissues and report compartment-specific outcomes.

The next phase of research should establish the durability and clinical relevance of the retention advantage and determine which product, dose, preparation method, and indication provide the greatest benefit. Direct randomized comparisons of mechanical SVF, enzymatic SVF, expanded ADSCs, PRP, and conventional fat under standardized harvesting and injection protocols would be particularly informative. Reporting should include viable-cell dose, cellular phenotype, platelet and leukocyte counts, injected volume, anatomical plane, processing time, and sterility controls to improve reproducibility and clinical transferability.

Future trials should also report effect sizes and confidence intervals, use analyses appropriate for split-face or split-treatment designs, prespecify primary time points, and distinguish absolute retained volume from percentage retention. These measures would improve clinical interpretation and facilitate quantitative synthesis. Longer follow-up is required to determine whether the demonstrated six- to 12-month advantages persist and reduce the need for repeat grafting.

Overall, the evidence is strongest for cellular enrichment, less consistent for PRP, and does not support routine combined SVF-PRP supplementation. Further work should define the magnitude, durability, and patient-centered value of the observed benefit using standardized protocols and outcome measures.

Conclusions

This systematic review indicates that SVF- and ADSC-enriched facial fat grafting can improve objective volume retention during short-term follow-up, with a favorable tolerability profile in prospective comparative studies. The evidence is more consistent for cellular enrichment than for PRP, while combined SVF-PRP strategies have not demonstrated an incremental benefit.

The available studies do not identify a single optimal preparation or universal clinical indication. Future research should standardize product characterization, dosing, anatomical targets, and outcome assessment and determine whether the observed benefits persist over longer follow-up.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Manuel Neiva-Sousa, Maria Luísa Sequeira, Tatiana Antunes

Critical review of the manuscript for important intellectual content: Manuel Neiva-Sousa, Tatiana Antunes

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Disclosures

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