Stromal Vascular Fraction–Enriched vs Standard Fat Grafting for Breast Reconstruction and Augmentation: A Prospective Multicenter Comparative Randomized Study

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Abstract

Background: Autologous fat grafting (AFG) has become a technique in aesthetic and reconstructive breast surgery. However, graft retention remains variable and requires repeated procedures. Stromal vascular fraction (SVF) enrichment has been proposed to improve graft survival through angiogenesis and tissue integration, although comparative evidence remains limited.

Objectives: The endpoint was MRI-based graft retention at 12 months. Secondary outcomes included 24-month retention, complications, BREAST-Q outcomes, radiologic findings, and revision procedures. MRI volumetric assessment was performed using 3-dimensional segmentation protocols and analyzed by breast radiologists.

Methods: A multicenter, randomized controlled study was conducted across 6 centers between January 2021 and March 2025. Patients affected by bilateral breast hypoplasia, breast asymmetry associated with unilateral breast hypoplasia, breast ptosis/pseudoptosis, and postlumpectomy defects were randomized to standard AFG or SVF-enriched AFG.

Results: Three hundred and twelve patients were randomized (156 per group). Follow-up was 28.6 ± 6.4 months. At 12 months, MRI graft retention was greater in the SVF-enriched group compared with standard fat grafting (71.8% ± 11.2% vs 56.4% ± 13.7%; $P < .001$). Retention persisted at 24 months (66.2% ± 12.0% vs 49.8% ± 14.1%; $P < .001$). BREAST-Q scores were higher in the SVF group at both follow-up intervals. Fat necrosis and oil cyst formation rates were similar between groups. No suspicious MRI findings attributable to fat grafting were identified during follow-up.

Conclusions: SVF-enriched AFG demonstrated improved volumetric persistence and higher patient-reported satisfaction compared with standard AFG, without increased radiologic or clinical complications. MRI-based evaluation may improve reproducibility in future breast fat grafting studies.

Level of Evidence: 1 (Therapeutic)

Autologous fat grafting (AFG) has evolved into a central modality in regenerative plastic surgery for breast augmentation, contour correction, congenital deformities, and secondary breast reconstruction.[1-4] The technique offers several advantages over implant-based surgery, including the absence of permanent foreign material, natural tissue consistency, simultaneous body contouring, and reduced implant-related complications.[5-7] Despite increasing clinical acceptance, long-term graft survival remains unpredictable. Adipocyte ischemia, inadequate neovascularization, inflammatory remodeling, and variable recipient-site vascularity contribute to partial fat resorption and volume instability.[8,9] Reported long-term retention rates range from 40% to 80%, depending on harvesting technique, processing protocols, recipient-site compliance, and imaging methodology.[10-12] The stromal vascular fraction (SVF) contains adipose-derived stromal cells, endothelial progenitors, pericytes, macrophages, and regenerative cytokines that promote

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angiogenesis and adipocyte survival.[13-15] Experimental and clinical investigations suggest that SVF enrichment may improve graft integration through enhanced neovascularization and reduced ischemic apoptosis.[16-18] However, available evidence remains heterogeneous and limited by retrospective methodology, inconsistent imaging protocols, and lack of multicenter randomization. MRI currently represents the most accurate imaging modality for volumetric quantification after fat grafting because of superior soft-tissue discrimination and reproducibility.[19-21] Nevertheless, few studies have implemented standardized MRI-based multicenter protocols.

We hypothesized that SVF-enriched AFG would demonstrate superior long-term volumetric persistence compared with standard AFG while maintaining comparable complication and radiologic safety profiles. Therefore, the present multicenter randomized controlled study was designed to compare SVF-enriched vs standard AFG using standardized MRI volumetric analysis.

METHODS

Study Design

This prospective, multicenter (Italy and Greece), single-blind (outcome assessors and statisticians blinded) randomized controlled study was conducted in accordance with CONSORT 2010 guidelines (Supplemental Figure 4, available online at https://doi.org/10.1093/asj/sjag197), the CONSORT checklist (Appendix), the Declaration of Helsinki, and internationally recognized ethical standards for clinical research.[22] All procedures were performed in compliance with European regulatory frameworks governing advanced therapy medicinal products, including Regulation (EC) no. 1394/2007 and guidance issued by the European Medicines Agency Committee for Advanced Therapies (EMA/CAT/600280/2010 Rev. 1). The study was not prospectively registered in a public clinical trial registry.

The investigational SVF-enrichment procedure was performed using a mechanical isolation system based on filtration and centrifugation without in vitro expansion. In accordance with EMA/CAT guidance and the Guideline on Human Cell-Based Medicinal Products (2015, section 2.2.4a), this process was classified as "minimal manipulation," as it did not alter the biological characteristics or structural integrity of the cellular components.

The study protocol was developed under a contractual research agreement and conducted as part of an institutional research project (IRB) approved by the relevant academic department (approval no. E83C22001960005).

Patient Selection

Patient selection was performed according to specific inclusion and exclusion criteria. Demographic characteristics, such as age, gender, race, and breast indication (cosmetic augmentation or reconstructive indication), as well as details regarding the intervention/comparator, outcomes, study design, and eligibility criteria, were collected and described following the PICOS approach. These data are summarized in Table 1.

Patients were considered eligible for the study if they were between 18 and 60 years of age, were candidates for breast augmentation, breast asymmetry/ptosis corrections, or breast reconstruction procedures with AFG, and presented an adequate amount of donor adipose tissue. Clinical indications (Supplemental Figure 4) included bilateral breast hypoplasia (Figure 1A-C; Supplemental Figure 2A-C, available online at https://doi.org/10.1093/asj/sjag197; mild degree, $n = 65$; moderate degree, $n = 54$; severe degree, $n = 33$), breast asymmetry associated with unilateral breast hypoplasia (Figure 2A-C; mild degree, $n = 20$; moderate degree, $n = 24$; severe degree, $n = 13$), breast ptosis/pseudoptosis (mild degree, $n = 26$; moderate degree, $n = 21$), and postlumpectomy defects ($n = 56$). Participants were required to have a BMI between 18 and 30 kg/m^2 and to agree to undergo MRI follow-up for 24 months.

Table 1. Baseline Demographic and Clinical Characteristics

Characteristic	Standard AFG ($n = 156$)	SVF-enriched AFG ($n = 156$)	*P*-value
Age (years)	34.7 ± 8.5	34.9 ± 8.7	.82
BMI (kg/m^2)	23.8 ± 3.2	24.0 ± 3.0	.64
Smoking (%)	18.5	17.9	.88
Indication (%)			.91
Aesthetic augmentation	52	50	
Asymmetry and ptosis	31	32	
Postlumpectomy	17	18	
Injected volume (mL)	274 ± 74	262 ± 34	.42

AFG, autologous fat grafting; SVF, stromal vascular fraction.

Patients were excluded from the study if they had an active malignancy, uncontrolled diabetes, or an autoimmune disease. Additional exclusion criteria included smoking more than 10 cigarettes per day, a history of breast irradiation within the previous 12 months, previous silicone implant rupture, as well as pregnancy or breastfeeding at the time of enrollment.

Randomization

Patients were randomized in a 1:1 ratio using a computer-generated block randomization sequence stratified by participating center. Allocation concealment was achieved using sequentially prepared sealed opaque envelopes. Because of the nature of the intervention, surgeons could not be blinded. MRI radiologists performing volumetric assessments and statistical analysts remained blinded to treatment allocation throughout the analysis.

Sample Size Calculation

Sample size analysis demonstrated that 138 patients per group were required to detect a 10% difference in MRI-based graft retention between groups with 80% statistical power and a 2-sided α level of .05. Assuming a 10% dropout rate, a total enrollment target of 312 patients was established.

Surgical Technique

Fat Harvesting

Adipose tissue harvesting was performed through 50 mL Luer–Lok syringes using a low-pressure suction technique to minimize trauma to adipocytes and preserve cell viability. Before harvesting, the donor sites were infiltrated with a tumescent solution, after which fat was aspirated using 3 mm blunt cannulas. Common donor sites included the abdomen, flanks, and lateral thighs.

Fat Processing

For the standard AFG group, the harvested adipose tissue was processed according to the Coleman technique, which involved

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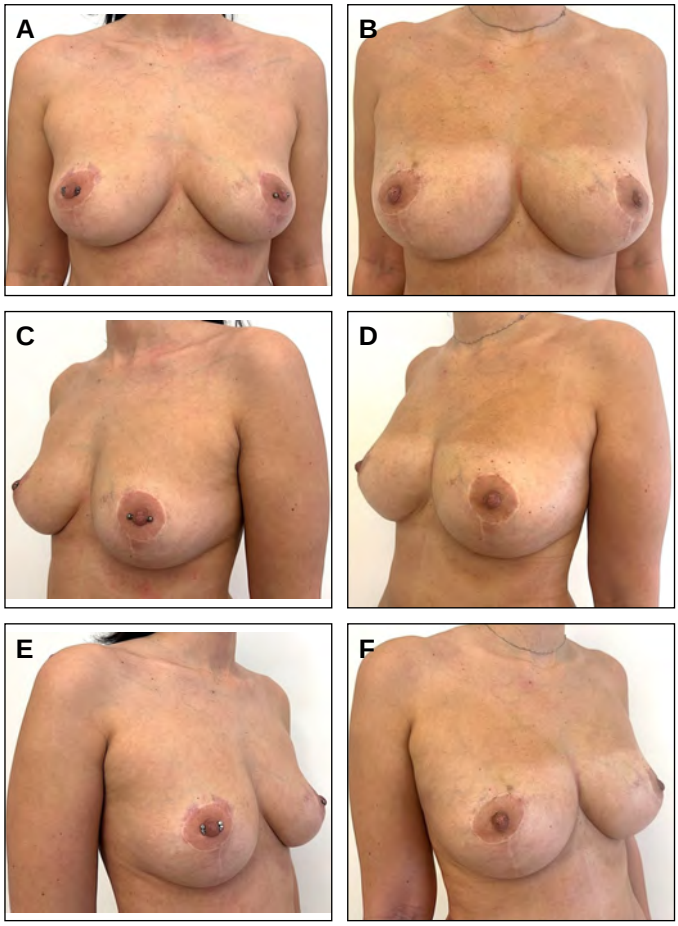


Figure 1. A 31-year-old female affected by outcomes of previous mastopexy, loss of volume, and ptosis, treated with stromal vascular fraction–enriched autologous fat grafting for aesthetic purposes. (A) Preoperative projection in frontal view. (B) Postoperative projection in frontal view, after 12 months, evidencing Improvement of the breast volume and shape, tissue elasticity, with reduction of ptosis. (C) Preoperative projection in ¾ left view. (D) Postoperative projection after 12 months in ¾ left view. (E) Preoperative projection in ¾ right view. (F) Postoperative projection after 12 months in ¾ right view.

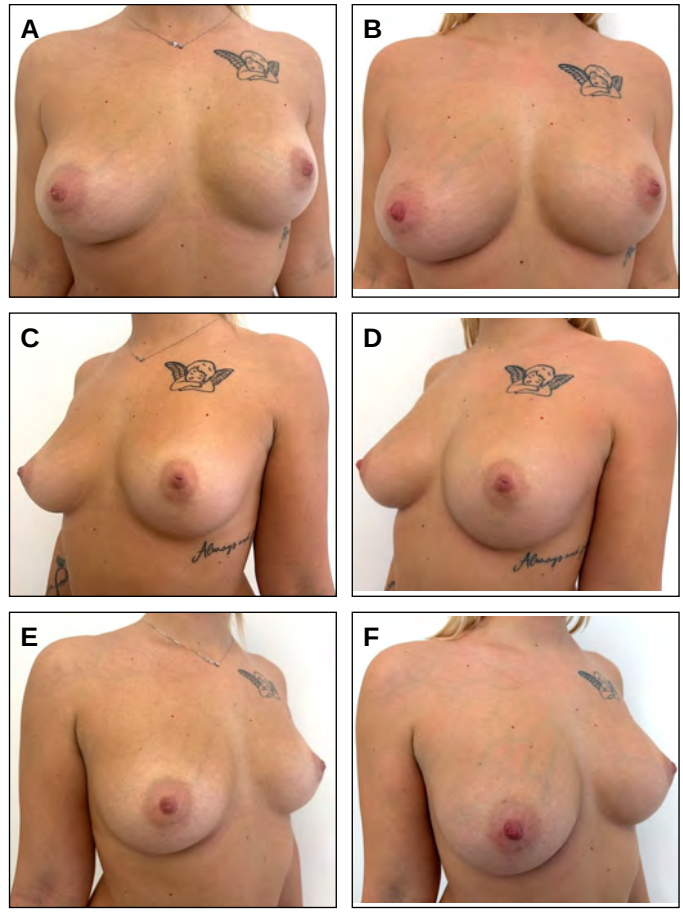


Figure 2. A 21-year-old female affected by breast asymmetry and loss of volume (especially in the left breast), treated with stromal vascular fraction–enriched autologous fat grafting for aesthetic purposes. (A) Preoperative projection in frontal view. (B) Postoperative projection in frontal view, evidencing all the improvements. (C) Preoperative projection in ¾ left view. (D) Postoperative projection after 24 months in ¾ left view. Improvement in breast volume and shape (especially in the left breast), tissue elasticity, and reduction of asymmetry. (E) Preoperative projection in ¾ right view. (F) Postoperative projection after 24 months in ¾ right view.

centrifugation at 1200 × *g* for 3 min to separate viable fat from oil, blood, and other unwanted components.[1,23]

In the SVF-enriched AFG group, 60 mL of adipose tissue was harvested using a 10 mL Luer–Lok syringe equipped with a 3 mm dual-port cannula and processed using a Microlyzer SVF t-lab kit (t-lab Esentepe Mah. Büyükdere Cd. No:151 Yonca Apt. C Blok No:42 Şişli, İstanbul https://tlab.com.tr/en/ continued in D-MED CELLANOVA kit, D-MED GRUP MEDİKAL, Üçevler Mah. 70. Sk. İbrahim Yazıcı Plaza-1 No:1/22d Nilüfer, Bursa, Turkey). The lipoaspirate was allowed to decant vertically for ~5 min to facilitate separation between the lower aqueous fraction, containing tumescent fluid and blood, and the upper adipose layer. The infranatant fluid was discarded until ~40 mL of adipose tissue remained. The adipose tissue was then transferred into 10 mL syringes and centrifuged at 1500 × *g* for 8 min. Following centrifugation, 3 layers were identified: a superficial oil layer, an intermediate condensed adipose layer, and a lower layer containing blood and residual tumescent solution. Only the intermediate condensed adipose fraction was retained. The condensed adipose tissue subsequently underwent progressive mechanical micronization by repeated inter-syringe passage through sequential blade filters of decreasing pore size (2400 µm, 31 passages; 1200 µm, 31 passages; and 600 µm, 101 passages). The mechanically processed tissue was then mixed with saline solution, agitated, and centrifuged again at 400 × *g* for 10 min. This second centrifugation generated 3 distinct fractions: an upper triglyceride layer, an intermediate extracellular matrix layer, and a lower SVF pellet suspended in saline. Using an 18-G needle and syringe, the SVF pellet was carefully collected after resuspension in saline. The resulting cell suspension was subsequently filtered through a 41 µm filter to remove residual debris and obtain a homogeneous cellular suspension. Before SVF enrichment, the adipose graft intended for transplantation underwent additional purification through dedicated washing and filtration procedures to remove residual blood, oil, cellular debris, and inflammatory contaminants, thereby obtaining purified fat graft material. Subsequently, SVF was added to the purified adipose graft at a ratio of 0.1 mL SVF per 1 mL purified fat. The final SVF-enriched graft demonstrated a mean concentration of 1.8×10^6 nucleated cells/mL as quantified by flow cytometry.

Injection Technique

Fat grafting was performed using a previously described multilayer microdroplet technique with retrograde injection through multiple tissue tunnels.[16,24,25] This method was selected to optimize graft survival by maximizing contact with the recipient-site vasculature and promoting homogeneous fat distribution. Fat was injected into the subcutaneous and intraglandular planes while avoiding direct

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Table 2. MRI Graft Retention Over Time

Time point, months	Standard AFG	SVF-enriched AFG	Mean difference (95% CI)	*P*-value
6	63.2 ± 12.8	77.1 ± 10.6	13.9 (10.2-17.6)	<.001
12	56.4 ± 13.7	71.8 ± 11.2	15.4 (11.2-19.6)	<.001
24	49.8 ± 14.1	66.2 ± 12.0	16.4 (12.0-20.8)	<.001

AFG, autologous fat grafting; SVF, stromal vascular fraction.

intraductal placement. Each breast was modeled geometrically as a cone.[16,25] Accordingly, the initial breast volume was estimated using the formula: $V = \pi \times r^2 \times h/3$, where r represents the breast base radius and h the breast height (Supplemental Figure 3, available online at https://doi.org/10.1093/asj/sjag197). The planned graft volume was then tailored according to the patient's aesthetic goals, the calculated baseline breast volume, and the amount of available fat. The target injection volume corresponded approximately to the calculated initial breast volume, with the same numerical value expressed in milliliters of injected fat and cubic centimeters of breast volume.[16,25]

Magnetic Resonance Imaging (MRI) Protocol

MRI served as the primary modality for volumetric assessment throughout the study. To ensure consistency and reproducibility across participating institutions, all MRI examinations were performed using standardized 3-T breast MRI systems (MAGNETOM Skyra, Siemens Healthineers, Erlangen, Germany) with T_1-weighted and fat-suppression sequences. Patient positioning was standardized and maintained consistently across imaging sessions. Volumetric measurements therefore represent standardized MRI-derived breast volumes rather than upright clinical breast projection. This approach was applied identically at baseline and at all postoperative time points and in both treatment groups.

Volumetric analysis was performed using OsiriX MD software (Pixmeo SARL, Bernex, Switzerland) with semi-automated 3-dimensional segmentation protocols. MRI examinations were performed at baseline (Supplemental Figure 1A, available online at https://doi.org/10.1093/asj/sjag197) and subsequently at 6, 12, and 24 months postoperatively. Volumetric analyses were independently conducted by 2 blinded breast radiologists. Interobserver reliability was evaluated using the intraclass correlation coefficient (ICC).

All MRI examinations were performed with the patient in the standardized supine position. Consequently, the reported volumetric measurements represent supine MRI-derived breast volumes and should not be interpreted as direct measures of upright breast projection.

Outcomes

Primary Outcome

The primary endpoint of the study was the percentage of graft retention assessed by MRI at 12 months following surgery.

Secondary Outcomes

Secondary outcomes included MRI-based graft retention at 24 months, patient-reported satisfaction assessed using the BREAST-Q questionnaire, postoperative complications, radiologic abnormalities, the number of grafting sessions required, and the need for revision surgery.

Statistical Analysis

Continuous variables were summarized as mean ± standard deviation, whereas categorical variables were presented as frequencies and percentages. The distribution of continuous variables was assessed using the Shapiro–Wilk test. Between-group comparisons were performed using Student's *t*-test for normally distributed continuous variables and the Mann–Whitney *U* test for non-normally distributed variables. Categorical variables were compared using the χ^2 test or Fisher's exact test, as appropriate.

Longitudinal MRI-derived volumetric measurements were analyzed using linear mixed-effects models for repeated measures, including treatment group, time, and the treatment-by-time interaction as fixed effects and a patient-specific random intercept to account for within-subject correlation. Model assumptions were assessed by inspection of residual Q–Q plots and evaluation of model fit using the Akaike information criterion. Variance inflation factors were examined to assess potential multicollinearity among covariates included in multivariable models.

Multivariable linear regression was used to identify independent predictors of 12-month graft retention. The primary model included prespecified treatment- and patient-level variables that were consistently available across the study cohort, including age, BMI, injected volume, SVF enrichment, and recipient indication. Smoking status, donor site, and previous breast surgery were not included in the primary model because of heterogeneity in their distribution across clinical indications and the potential risk of model overparameterization.

The primary analysis was based on the intention-to-treat population. No prespecified sensitivity or per-protocol efficacy analyses were performed. Missing data were handled using multiple imputation by chained equations. Interobserver agreement for MRI volumetric measurements was assessed using the ICC and Bland–Altman analysis.

Statistical analyses were performed using SPSS version 29.0 (IBM Corp.), R version 4.3, and GraphPad Prism version 10. Statistical significance was defined as a 2-sided *P*-value <.05. No adjustment for multiple comparisons was applied because secondary and exploratory outcomes were considered hypothesis-generating.

RESULTS

Patient Demographics

A total of 312 female participants were randomized; of these, 298 patients completed a 12-month follow-up, and 287 completed a 24-month MRI evaluation. Reasons for loss to follow-up included pregnancy, relocation, and withdrawal of consent. The mean patient age was 34.8 ± 8.6 years, whereas the mean BMI was 23.9 ± 3.1 kg/m^2. Clinical indications were similarly distributed between treatment groups, with aesthetic augmentation representing 52% of cases in the standard AFG group and 50% in the SVF-enriched group, asymmetry and ptosis representing 31% and 32%, respectively, and postlumpectomy reconstruction representing 17% and 18%, respectively ($P = .91$). No statistically significant differences in baseline demographic characteristics (Table 1) were identified between the treatment groups.

MRI Volumetric Outcomes

MRI volumetric analysis demonstrated significantly greater graft retention in the SVF-enriched AFG group compared with the standard AFG group at all postoperative follow-up intervals (Table 2 and Supplemental Table 1, available online at https://doi.org/10.1093/asj/sjag197).

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Table 3. Postoperative Complications

Complication	Standard AFG (n = 156), %	SVF group (n = 156), %	Risk difference, %	P-value
Fat necrosis	8.9	5.1	+3.8	.18
Oil cysts	6.4	4.5	+1.9	.42
Infection	1.9	1.3	+0.6	.65
Seroma	3.2	2.6	+0.6	.77

AFG, autologous fat grafting; SVF, stromal vascular fraction.

At 6 months, mean graft retention was 63.2% ± 12.8% in the standard AFG group and 77.1% ± 10.6% in the SVF-enriched group (P < .001), with a mean between-group difference of 13.9% (95% CI, 10.2%-17.6%).

At 12 months, retention values decreased to 56.4% ± 13.7% in the standard AFG group, whereas the SVF-enriched group maintained significantly higher retention rates of 71.8% ± 11.2% (P < .001), with a mean between-group difference of 15.4% (95% CI, 11.2%-19.6%).

Similarly, at 24 months, graft retention remained superior in the SVF-enriched group, with mean retention rates of 66.2% ± 12.0% compared with 49.8% ± 14.1% in the standard AFG group (P < .001), corresponding to a mean between-group difference of 16.4% (95% CI, 12.0%-20.8%).

Linear mixed-effects analysis demonstrated a significant treatment-by-time interaction (F = 16.84, P < .001), indicating that SVF enrichment significantly influenced long-term volumetric stability. Interobserver agreement was excellent (ICC = 0.94; 95% CI, 0.91-0.96).

Complications

The overall complication rate was 18.6% in the standard AFG group and 14.1% in the SVF-enriched AFG group. Fat necrosis occurred in 8.9% of patients receiving standard AFG compared with 5.1% in the SVF-enriched group, although this difference did not reach statistical significance (P = .18; Table 3).

Similarly, oil cyst formation was observed in 6.4% and 4.5% of patients in the standard and SVF-enriched groups, respectively (P = .42). Importantly, no cases of severe infection, pulmonary embolism, or oncologic adverse events were reported during the follow-up period.

Infection occurred in 1.9% of patients in the standard AFG group and 1.3% in the SVF-enriched group (P = .65), whereas seroma occurred in 3.2% and 2.6%, respectively (P = .77). No statistically significant between-group differences were observed for any individual complication.

Radiologic Outcomes

MRI examinations demonstrated only benign postoperative radiologic findings, including fat necrosis, oil cysts, and stable calcifications. No suspicious enhancement patterns suggestive of malignancy attributable to AFG were identified. Furthermore, no BI-RADS 5 lesions were detected throughout the study period.

BREAST-Q Outcomes

Patient-reported outcomes assessed using the BREAST-Q questionnaire demonstrated significantly higher satisfaction scores in the SVF-enriched AFG group compared with standard AFG at both postoperative follow-up intervals (Table 4). At 12 months, the overall BREAST-Q score was significantly higher in the SVF-enriched cohort (82.6 ± 8.2) compared with the standard AFG group (74.1 ± 9.4; mean difference, 8.5 points; 95% CI, 6.3-10.7; P < .001). Similarly, at 24 months, satisfaction remained superior in the SVF-enriched group (80.4 ± 8.9 vs 71.3 ± 10.2; mean difference, 9.1 points; 95% CI, 6.7-11.5; P < .001). At 24 months, BREAST-Q data were available for 149 patients in the standard AFG group and 138 patients in the SVF-enriched group. The largest intergroup differences were observed in satisfaction with breasts, surgical outcome, and sexual well-being, reflecting improved long-term volume stability, contour maintenance, and overall aesthetic perception after SVF enrichment. Mixed-effects longitudinal analysis confirmed a significant treatment-by-time interaction (P < .001), supporting sustained superiority of SVF-enriched grafting throughout follow-up.

Multivariate Regression Analysis

Multivariable regression analysis demonstrated that SVF enrichment was independently associated with greater graft retention (β = .29; 95% CI, 0.18-0.41; P < .001). Higher BMI was negatively associated with graft retention (β = −.17; 95% CI, −0.31 to −0.02; P = .03). Age (β = −.05; 95% CI, −0.12 to 0.02; P = .18), injected volume (β = .11; 95% CI, −0.03 to 0.25; P = .12), and indication (reconstructive vs aesthetic; β = −.09; 95% CI, −0.21 to 0.04; P = .16) were not significantly associated with 12-month graft retention (Table 5).

DISCUSSION

AFG has evolved into a major regenerative strategy in aesthetic and reconstructive breast surgery because of its ability to restore natural breast volume and contour without permanent foreign materials.[1-6] Despite increasing clinical acceptance, long-term graft survival remains unpredictable because of ischemia-induced adipocyte loss, inflammatory remodeling, and variability in recipient-site vascularization.[8-10,15,26]

The present multicenter randomized study demonstrated that SVF-enriched fat grafting achieved significantly greater long-term volumetric persistence than standard AFG, while maintaining comparable complication rates and radiologic safety profiles. MRI-based graft retention remained consistently higher in the SVF-enriched cohort throughout the study period, and patient satisfaction was significantly higher at the prespecified follow-up assessments.

These findings are consistent with previous experimental and clinical investigations suggesting that SVF-containing adipose tissue may enhance angiogenesis, vascular integration, and adipocyte survival through regenerative cellular signaling.[4,6,13-18] In particular, Yoshimura et al, Eto et al, and Kølle et al reported improved graft persistence following cell-assisted lipotransfer and adipose-derived stromal-cell enrichment.[4,7,15,18] However, the broader literature on cell-assisted fat grafting remains heterogeneous. Previous studies have reported variable or less pronounced effects depending on adipose harvesting and processing techniques, SVF isolation methods, cellular characterization, cell dose, injection technique, recipient-site characteristics, imaging methodology, and follow-up duration.[8,10,18,21,27-30] The randomized placebo-controlled experience reported by Kølle et al provided evidence supporting improved graft survival following adipose-derived stromal-cell enrichment, whereas systematic reviews of breast fat grafting have emphasized substantial variability in graft retention and processing methodologies.[7,8,10,18,21,27,29] Therefore, direct comparison across

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Table 4. BREAST-Q Satisfactions Scores

BREAST-Q domain	Standard AFG	SVF-enriched AFG	Mean difference	95% CI	*P*-value	Time point, months
12 months						
Satisfaction with breasts	73.8 ± 9.6	83.5 ± 8.1	9.7	7.7-11.7	<.001	12
Satisfaction with surgical outcome	74.5 ± 8.8	84.2 ± 7.9	9.7	7.8-11.6	<.001	12
Psychosocial well-being	76.1 ± 9.1	84.7 ± 7.8	8.6	6.7-10.5	<.001	12
Sexual well-being	71.4 ± 10.3	80.8 ± 9.0	9.4	7.3-11.5	<.001	12
Physical well-being (chest)	74.6 ± 8.7	79.9 ± 8.1	5.3	3.4-7.2	.002	12
24 months						
Satisfaction with breasts	70.9 ± 10.5	81.7 ± 8.6	10.8	8.6-13.0	<.001	24
Satisfaction with surgical outcome	71.8 ± 9.7	82.4 ± 8.4	10.6	8.5-12.7	<.001	24
Psychosocial well-being	73.5 ± 9.9	83.1 ± 8.0	9.6	7.5-11.7	<.001	24
Sexual well-being	68.7 ± 10.8	79.6 ± 9.1	10.9	8.6-13.2	<.001	24
Physical well-being (chest)	72.4 ± 8.9	78.2 ± 8.3	5.8	3.8-7.8	.001	24
Overall mean score						
Mean value at 12 months	74.1 ± 9.4	82.6 ± 8.2	8.5	6.6-10.4	<.001	12
Mean value at 24 months	71.3 ± 10.2	80.4 ± 8.9	9.1	7.0-11.2	<.001	24

AFG, autologous fat grafting; SVF, stromal vascular fraction.

studies remains challenging, and the present multicenter MRI-based data should be interpreted as contributing to, rather than resolving, the methodological heterogeneity of the existing literature.

Several biological mechanisms may plausibly contribute to the greater persistence observed after SVF-enriched grafting. SVF contains stromal cells, endothelial progenitor populations, pericytes, macrophages, and extracellular signaling components that may promote angiogenesis, vascular maturation, extracellular matrix remodeling, and tissue integration.[4,6,13-18] Enhanced early vascularization may reduce the duration of ischemia experienced by transplanted adipocytes and thereby limit subsequent necrosis and resorption. Nevertheless, because the SVF-enriched group underwent additional washing, filtration, mechanical processing, centrifugation, and SVF isolation beyond the Coleman-type processing used for standard AFG, the present trial cannot determine which individual cellular component or processing step was responsible for the observed benefit. Accordingly, the biological interpretation should remain cautious, and the findings should be considered evidence supporting the clinical potential of the complete SVF-enriched processing pathway rather than definitive evidence of an isolated SVF-mediated effect.

An important strength of the present study is its multicenter randomized design combined with standardized MRI-based volumetric assessment. MRI provides reproducible volumetric measurements and superior soft-tissue discrimination compared with ultrasound or photographic assessment.[10,19-21] Previous investigations have frequently relied on photographic evaluation, ultrasound, mammography, or subjective clinical estimation, thereby limiting reproducibility and inter-study comparability.[10-12] Choi et al and Herly et al previously demonstrated the reliability of MRI-based volumetric analysis after breast fat grafting.[10,19,20] The excellent interobserver agreement observed in the present study further supports the robustness of the imaging methodology. Standardized multicenter MRI protocols may therefore provide an important framework for improving reproducibility and facilitating comparison across future regenerative breast surgery studies.

Radiologic safety remains an important consideration in breast fat grafting. Historically, postoperative fat necrosis, calcifications, and oil cysts have raised concerns regarding potential interference with breast cancer screening.[11,21,31] In the present study, imaging findings remained benign, with no suspicious enhancement patterns or evidence of oncologic events attributable to the grafting procedure during the study follow-up. These findings are consistent with previous studies and meta-analyses supporting the radiologic safety and reassuring oncologic profile of breast lipofilling.[29,31-34] Nevertheless, these findings should not be interpreted as establishing long-term oncologic safety, and extended surveillance remains warranted, particularly in patients with a history of breast malignancy.[32-34]

Patient-reported outcomes also favored SVF enrichment, with significantly higher BREAST-Q satisfaction scores at 12 and 24 months. These findings are consistent with previous studies reporting high patient satisfaction following breast fat grafting,[16,24,25] potentially reflecting natural tissue consistency, improved breast contour, and the absence of implant-related morbidity associated with autologous tissue augmentation.[23,29,35-39] Importantly, in the present cohort, the greater long-term volumetric persistence observed in the SVF-enriched group was accompanied by consistently higher patient-reported satisfaction, suggesting that the between-group difference in graft retention may have had clinically relevant implications beyond the MRI-derived volumetric measurements. However, MRI-based graft retention should not be interpreted as a surrogate for avoidance of revision surgery. Whether SVF enrichment ultimately reduces the need for repeat fat grafting or other revision procedures remains to be established and would require dedicated analyses of revision-free survival, cumulative grafting procedures, and long-term aesthetic outcomes.

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Table 5. Predictors of Graft Retention (12 Months)

Variable	β coefficient	95% CI	*P*-value
SVF enrichment	0.29	0.18 to 0.41	<.001
BMI	−0.17	−0.31 to −0.02	.03
Age	−0.05	−0.12 to 0.02	.18
Injected volume	0.11	−0.03 to 0.25	.12
Indication (reconstructive vs aesthetic)	−0.09	−0.21 to 0.04	.16

SVF, stromal vascular fraction.

From a practical perspective, SVF enrichment is more technically complex than standard AFG and requires additional equipment, processing time, operator expertise, and quality-control procedures. These requirements may increase operative and institutional costs. Because the present study did not include a formal cost-effectiveness analysis, it cannot establish whether the additional expenditure associated with SVF enrichment is justified by the magnitude of the clinical benefit. In addition, regulatory requirements for cell-processing procedures may vary according to jurisdiction, processing methodology, intended clinical use, and the degree of manipulation of the cellular product. Accordingly, implementation of SVF-enriched AFG requires appropriate institutional regulatory oversight and standardized quality-control procedures.

Several limitations should be acknowledged. First, the study population included heterogeneous clinical indications, including aesthetic augmentation, breast asymmetry and ptosis, and postlumpectomy reconstruction. These conditions differ in recipient-site anatomy, tissue vascularity, compliance, and previous surgical alteration and may therefore influence graft behavior. Although randomization was intended to balance these characteristics between treatment groups, indication-specific subgroup analyses were not prespecified, and the study was not powered to determine treatment effects within individual indications.

Second, although the multicenter design and center-stratified randomization enhance external validity and reduce the risk of systematic imbalance between treatment groups, complete standardization of surgical techniques, donor-site characteristics, postoperative management, and institutional practices across centers remains challenging. Because a fully adjusted center-level analysis was not available in the final analytical dataset, the possibility of residual or unmeasured institutional effects cannot be completely excluded.

Third, an important methodological limitation concerns the differences in fat-processing protocols between the treatment groups. The standard AFG group underwent Coleman-type processing, whereas the SVF-enriched group underwent additional washing, filtration, mechanical processing, centrifugation, and SVF isolation before enrichment. Thus, the present study evaluates the clinical effect of the complete SVF-enriched processing pathway rather than isolating the biological contribution of SVF itself. This distinction limits the extent to which the observed treatment effect can be attributed exclusively to SVF and should be considered when interpreting both the magnitude of the between-group difference and its mechanistic implications. Future randomized mechanistic studies should therefore standardize baseline fat processing between groups and introduce SVF enrichment as the only additional intervention.

Fourth, postoperative changes in body weight were not prospectively incorporated as a predefined covariate in the volumetric analysis. Because transplanted adipose tissue may undergo volume changes in response to systemic weight fluctuations, postoperative weight loss or gain may have contributed to interindividual variability in long-term graft retention. Consequently, the independent effect of body-weight changes on the observed volumetric outcomes cannot be determined.

Fifth, the progressive reduction in MRI-measured graft retention between 6 and 24 months should be interpreted in the context of the natural remodeling process following AFG, which includes early ischemic loss, subsequent revascularization, adipocyte remodeling, extracellular matrix turnover, and partial resorption. Accordingly, a reduction in retained volume over time does not necessarily indicate failure of the technique. Importantly, despite this temporal decline in both cohorts, the SVF-enriched group maintained consistently greater retained volume than the standard AFG group. Nevertheless, MRI volumetry was performed under standardized imaging positioning and does not fully reproduce the upright appearance of the breast. Differences in tissue compliance and positional deformation may therefore affect the relationship between MRI-derived volume and clinical breast projection. Mechanical factors, including external compression and postoperative bra use, may also theoretically influence graft distribution or apparent volume; however, these variables were not independently quantified in the present study. Because MRI was performed in the supine position, the measured volume may differ from the clinically perceived breast volume in the upright position. Supine positioning may alter the distribution of soft tissue and the apparent projection of the breast, particularly in patients with greater tissue compliance or ptosis. Therefore, MRI-derived volumetry should be interpreted primarily as a standardized measure of tissue volume rather than a direct surrogate for upright breast shape or projection

Sixth, the study excluded several higher-risk populations, including patients with BMI outside the predefined range, active malignancy, recent breast irradiation, uncontrolled diabetes, and other conditions associated with impaired wound healing or vascularity. The findings should therefore not be directly extrapolated to obese patients, recently irradiated tissues, active oncologic populations, or other recipients with impaired vascularity or altered tissue-healing capacity. Similarly, the inclusion of both aesthetic and reconstructive indications introduces clinical heterogeneity that may influence absolute graft retention. Longer-term oncologic surveillance remains warranted, particularly in patients with a history of breast malignancy.[32-34]

Finally, SVF processing increases procedural complexity, operative time, equipment requirements, and potentially overall treatment costs. Because a formal cost-effectiveness analysis was not performed, the additional clinical benefit associated with SVF enrichment cannot be fully weighed against its economic and logistical burden.

Taken together, these limitations warrant cautious interpretation of the findings but do not negate the consistently greater long-term volumetric retention and higher patient satisfaction observed in the SVF-enriched group. Rather, they underscore the need for further prospective studies to determine the independent biological contribution of SVF, assess the generalizability of these findings across different clinical populations, and define the clinical, regulatory, and economic implications of the complete SVF-enriched processing pathway. Future investigations should prioritize standardized cell-processing methodologies, harmonized multicenter MRI-based volumetric protocols, longer-term oncologic surveillance, artificial intelligence-assisted volumetric analysis, formal cost-effectiveness assessment, and large international registries capable of generating higher-level evidence.

CONCLUSIONS

SVF-enriched AFG was associated with greater long-term volumetric persistence and higher patient satisfaction compared with standard

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AFG within the limitations of this multicenter randomized study. Because the SVF-enriched group underwent additional adipose-tissue processing steps beyond those used for standard AFG, the observed benefit should be interpreted as the effect of the complete SVF-enriched processing pathway rather than as an isolated effect of SVF itself. Future randomized mechanistic studies should therefore standardize baseline fat-processing procedures between groups and introduce SVF enrichment as the only additional intervention to determine its independent biological contribution. Standardized multicenter MRI protocols may further improve the reproducibility and comparability of volumetric outcomes in regenerative breast surgery. Further research addressing long-term oncologic safety, standardized cell-processing methodologies, artificial intelligence-assisted MRI volumetry, cost-effectiveness, and international multicenter registries will be important to establish the broader clinical applicability and translational value of SVF-enriched fat grafting.

Supplemental Material

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