

## Review Article

# Supplementation of Facial Fat Grafting to Increase Volume Retention: A Systematic Review

Jan Aart M. Schipper, MD<sup>✉</sup>; Linda Vriend, MD<sup>✉</sup>; Aartje J. Tuin, MD, DMD, PhD; Pieter U. Dijkstra, PT, MT, PhD; Rutger H. Schepers, MD, DMD, MSc, PhD; Berend van der Lei, MD, PhD; Johan Jansma, MD, DMD, MSc, PhD, FEBOMFS; and Martin C. Harmsen, PhD<sup>✉</sup>

Aesthetic Surgery Journal  
2022, 1–17

© 2022 The Aesthetic Society.

This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial License (<https://creativecommons.org/licenses/by-nc/4.0/>), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact journals.permissions@oup.com

<https://doi.org/10.1093/asj/sjac122>  
[www.aestheticsurgeryjournal.com](http://www.aestheticsurgeryjournal.com)

**OXFORD**  
UNIVERSITY PRESS

## Abstract

**Background:** For decades, facial fat grafting has been used in clinical practice for volume restoration. The main challenge of this technique is variable volume retention. The addition of supplements to augment fat grafts and increase volume retention has been reported in recent years.

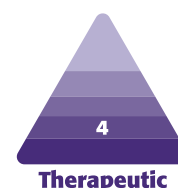
**Objectives:** The aim of this systematic review was to investigate which supplements increase volume retention in facial fat grafting as assessed by volumetric outcomes and patient satisfaction.

**Methods:** Embase, Medline, Ovid, Web of Science Core Collection, Cochrane Central Register of Controlled Trials, and Google Scholar were searched up to November 30, 2020. Only studies assessing volume after facial fat grafting with supplementation in human subjects were included. Outcomes of interest were volume or patient satisfaction. The quality of the studies was assessed with the Effective Public Health Practice Project tool.

**Results:** After duplicates were removed 3724 studies were screened by title and abstract. After reading 95 full-text articles, 27 studies were eligible and included for comparison. Supplementation comprised of platelet-rich plasma, platelet-rich fibrin, adipose tissue-derived stromal cells or bone marrow-derived stromal cells, cellular or tissue stromal vascular fraction, or nanofat. In 13 out of 22 studies the supplemented group showed improved volumetric retention and 5 out of 16 studies showed greater satisfaction. The scientific quality of the studies was rated as weak for 20 of 27 studies, moderate for 6 of 27 studies, and strong for 1 study.

**Conclusions:** It remains unclear if additives contribute to facial fat graft retention and there is a need to standardize methodology.

## Level of Evidence: 4



Editorial Decision date: May 5, 2022; online publish-ahead-of-print May 16, 2022.

Dr Schipper is a medical doctor and Dr Harmsen is a professor of cardiovascular regenerative medicine, Department of Pathology and Medical Biology, University of Groningen, University Medical Center Groningen, Groningen, the Netherlands. Dr Tuin is an oral and maxillofacial surgeon in training and Drs Schepers and Jansma are oral and maxillofacial surgeons, Department of Oral and Maxillofacial Surgery, University Medical Center Groningen, University of Groningen, Groningen, the Netherlands. Dr Vriend is a medical doctor and Dr van der Lei is a professor, Department of Plastic and Reconstructive Surgery, University Medical Center Groningen,

University of Groningen, Groningen, the Netherlands. Dr Dijkstra is a professor, Department of Rehabilitation Medicine, University Medical Center Groningen, University of Groningen, Groningen, the Netherlands.

## Corresponding Author:

Dr Martin C. Harmsen, Department of Pathology and Medical Biology, University of Groningen, University Medical Center Groningen, Hanzeplein 1-EA11, 9713 GZ Groningen, the Netherlands.

E-mail: [m.c.harmsen@umcg.nl](mailto:m.c.harmsen@umcg.nl)

Fat grafting has been performed in clinical practice since the end of the 19th century.<sup>1</sup> It has been used to restore volume loss due to trauma, aging, congenital defects, or for aesthetic reasons, predominantly in the face, breasts, and buttock. Facial fat grafting can be performed easily, safely, and with minimum donor-site morbidity and complications.<sup>2</sup> However, not all transplanted tissue is retained at the acceptor site. Long-term volume retention rates vary widely between 25% and 80%.<sup>3,5</sup> Additionally, multiple surgical procedures are often required to obtain the desired volume.

Lipografting is a form of tissue transplantation, albeit of fragmented adipose tissue. These fragments consist of multiple large lipid-laden adipocytes that are structurally supported by connective tissue and perfused with a highly developed microvasculature. Adipocytes are about 4-fold less numerous than stromal vascular cells, yet comprise about 90% of the total volume of fat.<sup>6</sup> Upon transplantation (ie, fat grafting), the survival and regeneration of adipocytes are pivotal to retaining the grafted volume.<sup>7</sup> Ischemia may cause apoptotic loss of adipocytes, and thus suppression of apoptosis in fat grafts might improve graft volume retention. For graft survival, it is essential to form a rapid connection between local vasculature and capillaries that literally stick out from the tissue clumps in the fat graft. Thus angiogenic stimulation by fat graft supplements is warranted. Any adipocytes lost from ischemic insult require replenishment through proliferation of pre-adipocytes (adipose tissue–derived stromal cells [ASCs]) and their differentiation and maturation into adipocytes, which would be supported by prometogenic factors in supplements. Finally, metabolic maintenance is important because adipocyte volume, ie, the storage of the high-energy triglycerides, varies with the body's metabolic demand. Weight loss is associated with loss of adipocyte volume and consequently with reduced graft volume.<sup>8</sup> Although repeated fat grafting does build up sufficient volume, this is an undesirable burden for the patient. Therefore, supplements that augment suppression of apoptosis, stimulate proliferation, and enhance angiogenesis are desired. In clinical applications, the cellular fate of grafted fat is usually not assessed, yet this does not preclude investigation of the influence of supplements on graft volume.

To increase graft retention, supplementation with several autologous components has been investigated. Blood-derived products, eg, platelet-rich plasma (PRP) and platelet-rich fibrin (PRF),<sup>9,10</sup> are a source of concentrated platelets, growth factors, and cytokines which could induce better graft retention by promoting angiogenesis and reducing apoptosis.<sup>11</sup> Adipose tissue–derived components, eg, ASCs, cellular and tissue stromal vascular fraction (cSVF, tSVF),<sup>12,13</sup> and nano- and microfat,<sup>14-16</sup> have shown proangiogenic action through paracrine factors which could induce better graft vascularization, reduce apoptosis, and increase proliferation.<sup>17,18</sup> Furthermore,

enzymatic cell-assisted lipografting made addition of cSVF or cultured ASC to fat grafting popular.<sup>4, 19-20</sup> However, because cell-assisted lipografting requires enzymatic digestion of SVF and the use of animal-derived enzymes such as collagenase it is restricted by legislation in many countries,<sup>21</sup> and hence new nonenzymatic, fast, intraoperative, mechanical dissociation procedures have been developed to produce tSVF.<sup>22,23</sup> PRP or PRF are also easily obtained by centrifugation of blood with or without anticoagulant.<sup>24</sup> These supplementations are believed to improve retention through either increased survival of the grafted cells by reducing/preventing cell apoptosis, or by restoring hypertrophy or increasing vascularization at the injection site.

Currently, the number of clinical studies investigating supplemented fat grafting is increasing rapidly, and multiple new supplementation therapies are being developed.<sup>25</sup> These developments warrant systematic evaluation of the clinical available evidence. The current systematic reviews on fat graft supplementation are heterogeneous because they include human and animal studies for various indications.<sup>26,27</sup> The aim of this systematic review was therefore to investigate the efficacy of human facial fat grafting based on quantitative volumetric outcome measures and patient satisfaction assessments.

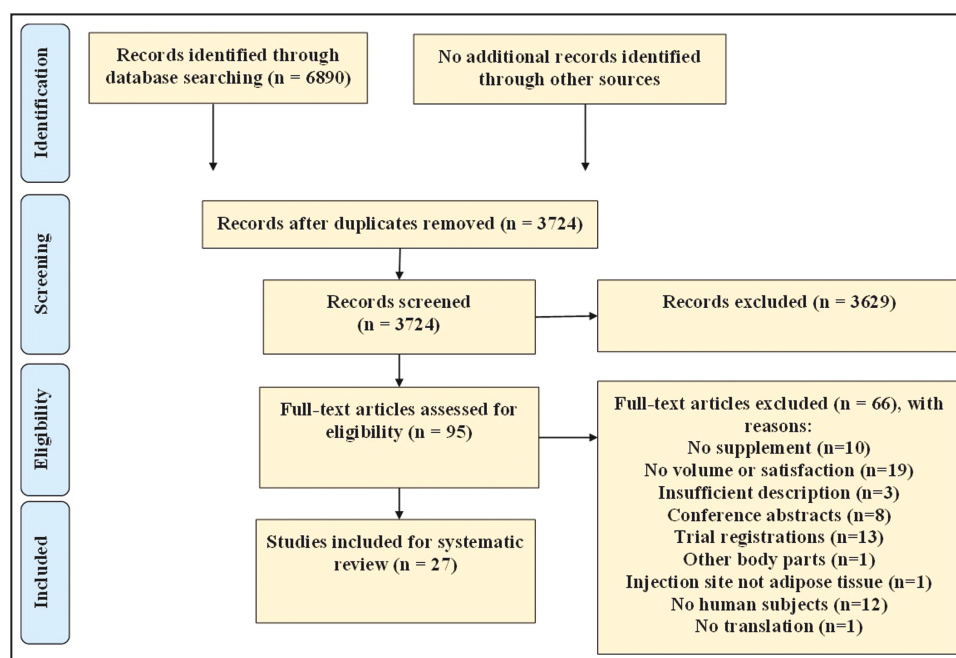
## METHODS

### Protocol and Registration

This manuscript follows the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement.<sup>28</sup> The study was registered in Prospero (register code: CRD42020179975).

### Search Strategy and Information Sources

A systematic literature search was conducted in the electronic medical databases Embase (Elsevier, Amsterdam, the Netherlands), MEDLINE (National Library of Medicine, Bethesda, MD), Ovid (Wolters Kluwer, Alphen aan den Rijn, the Netherlands), Web of Science Core Collection (Clarivate Analytics, London, UK), Cochrane Central Register of Controlled Trials (CENTER; London, UK), and Google Scholar (Google, Mountain View, CA) from inception to November 30, 2020. Search strategy was based on the PICO (population, intervention, comparison, outcome) framework and combined terms related to fat graft transplantation (ie, lipofilling, fat transplantation, adipose tissue transplantation, adipose tissue grafting, volume retention) plus a supplementation therapy (ie, PRP, ASCs, SVF, nanofat, microfat).<sup>29</sup> In databases where a thesaurus was available (Embase and MEDLINE), papers were searched by thesaurus terms and by title and/or abstract.



**Figure 1.** Flow diagram of study selection.

The searches were adapted corresponding to each database (Supplemental Table 1, available online at [www.aestheticsurgeryjournal.com](http://www.aestheticsurgeryjournal.com), and Figure 1). Reference lists of included studies were analyzed to identify relevant studies missed in the searches.

## Eligibility Criteria

Studies were included if they clinically evaluated the effects of fat grafting in combination with a supplement, for instance the addition of PRP, ASCs, or SVF, on volume restoration in the face or patient satisfaction. Only studies injecting in the adipose tissue plane in the face were included. Studies were excluded when no volumetric outcome was reported, as were studies reporting on other body parts than the face only. If studies described multiple body parts and data of the face were separately described, the study was included. (Systematic) reviews, case studies, conference abstracts, letters to the editor, and animal and in vitro studies were also excluded. No publication date restriction was applied.

## Study Selection and Data Collection Process

Two reviewers (J.S., L.V.) independently assessed titles, abstracts, and full texts. Disagreement between reviewers was discussed until consensus was reached. In the case of persistent disagreement, a senior author (M.H.) gave a binding verdict.

## Data Extraction

All data were extracted by the same 2 reviewers and consisted of 5 categories: study characteristics, treatment characteristics, complications, volumetric assessment of fat graft (retention), and patient satisfaction.

Complications were categorized as minor (erythema, mild edema, hematoma, local pain at incision site, and oily cyst) and major complications (infection, tissue loss, skin necrosis, fibrosis, severe edema, pain spreading beyond injection site, cellulitis, fat embolus, and embolus causing blindness). For supplemented fat grafting therapy, data outcomes of interest were time between harvesting and injection, injected volumes, supplement dosing, cell yield or PRP concentration, isolation procedures, repeated treatments, and characterization of supplementation therapy. For volumetric outcomes, data from objective and subjective volume measurement tools and follow-up points were extracted. When studies reported fat graft resorption as an outcome measure, retention was calculated as inverse resorption ( $100\% - x\%$ ). For each volume retention reported, a fold-change was calculated ( $\% \text{ supplemented fat divided by } \% \text{ fat}$ ). A difference was reported when there was a statistically significant difference ( $P < 0.05$ ).

## Risk of Bias in Individual Studies

The 2 reviewers independently assessed risk of bias with the Effective Public Health Practice Project tool (EPHPP).<sup>30</sup> This tool enables quality assessment of different types of

study design. Studies were given an overall final rating as strong, moderate, or weak based on ratings of study design, selection bias, confounders, data blinding, data collection, and dropouts. According to the EPHPP tool, “strong studies” had no weak rating, “moderate studies” had 1 weak rating and “weak studies” had 2 or more weak ratings.

## RESULTS

### Study Selection

In total, 3724 studies were identified. After title and abstract screening, 95 studies remained for full-text assessment of eligibility criteria (Figure 1). A total of 27 studies were included; 68 studies were excluded for the following reasons: 10 studies were excluded because the fat graft was not supplemented;<sup>23,31-39</sup> 19 studies were excluded because fat graft retention was not assessed by volumetric or patient satisfaction measurements;<sup>40-59</sup> 3 studies were excluded because the study methods or intervention were not evaluable due to insufficient description;<sup>60-62</sup> 8 studies were excluded because these were conference abstracts;<sup>63-69</sup> 13 studies were excluded because these concerned trial registrations;<sup>70-82</sup> 1 study was excluded because the supplementation therapy was not carried out in the face, but in other body parts;<sup>83</sup> in 1 study the injection site was not adipose tissue but product was injected within the muscles of the face (facial muscular plane);<sup>84</sup> 12 studies were excluded because they did not describe human subjects or clinical results;<sup>85-95</sup> no translation of 1 study was available (Russian).<sup>96</sup>

### Study Characteristics

The studies included were published between 2008 and 2020 (Table 1). Follow up ranged from 6 to 60 months and a total of 1117 participants were described in the studies (range, 6 to 236 per study). The mean age of the participants ranged between 6 and 61.5 years old and 73% of all patients were female (range, 33%-100%). Five studies had a female sex bias due to the inclusion of female participants only.<sup>97-101</sup> Eight studies reported mean BMI, which ranged from 17 to 32 kg/m<sup>2</sup>. Indications for supplemented fat grafting were with underlying pathology (48%) or cosmetic (without underlying pathology) with (19%) or without facelift (33%). Indications with underlying pathology were craniofacial deformity (31%), scars (23%), (hemi)facial lipoatrophy (15%), Parry-Romberg syndrome (15%), or a combination of these indications (15%). The majority (13/27) of the studies supplemented fat grafts with PRP/PRF. Three studies reported multiple supplements.<sup>102-104</sup> Studies were categorized by type of supplement (PRP, SVF, and cellular components) for analysis of supplement characteristics, volumetric, and patient satisfaction outcomes (Supplemental Table 2, available online at [www.aestheticsurgeryjournal.com](http://www.aestheticsurgeryjournal.com), and Tables 2, 3).

### Study Design and Quality

Study designs included randomized controlled trials (n = 6),<sup>67,99,101,105-107</sup> controlled trials (n = 6),<sup>4,19,108-111</sup> cohort studies (2 groups with pre- and posttreatment evaluation, n = 6),<sup>34,103,104,108,112,113</sup> cohort studies (1 group with pre- and posttreatment evaluation, n = 8)<sup>98,100,114-119</sup> and a retrospective study (n = 1)<sup>45</sup> (Table 4). Confounding factors were not controlled for in 8 studies.<sup>42,44,108,110,114,116-118</sup> The reliability and validity of outcome measurements were weak in 12 studies.<sup>4,19,44,67,105,108,110,113-116,119</sup> Four studies reported dropouts and reported the number of participants who completed the follow up.<sup>101,105,107,118</sup> Based on the EPHPP guidelines, 20 studies had an overall final rating of weak, 6 studies were rated as moderate, and only 1 study was rated as strong (4%).<sup>106</sup> Data pooling and meta-analysis was not possible due to heterogeneity across studies in terms of clinical features, eg, population characteristics, indications, supplementation strategies, and additional interventions (facelift, additional injections), and methodologic characteristics, eg, assessment tools, study design, and follow up.

### Characteristics of Supplementation Strategies

The mean injected total volume ranged from 6.8 to 100 mL. The volume-to-volume ratio of PRP-to-fat ranged from 1:2 to 1:9. In SVF-supplemented therapies, 2 out of 14 studies reported the ratio of supplementation. Repeated supplemented fat graft injections were performed in 11 studies and concerned merely supplementation with SVF and cellular components.<sup>19,34,108-113,115,117,118</sup> A minority of studies reported supplement concentrations: platelet concentration in PRP or PRF was  $0.8 \times 10^9$  to  $3.6 \times 10^9$ /mL (mean [standard deviation],  $2.6 [1.3] \times 10^9$ /mL), and the number of nucleated cells in cSVF or tSVF was  $0.3 \times 10^5$  to  $100 \times 10^5$  cells.<sup>112,107,109</sup> Some studies reported a concentration range of fat-supplemented therapy and the single addition of bone marrow-derived stromal cells (BMSCs) ranged from 3 to  $86 \times 10^8$  at a volume ratio of 2:1 of BMSC:fat graft.<sup>113</sup> Most studies performed intraoperative isolation procedures of the supplementation therapy. Two studies cultured ASCs for 14 days<sup>109</sup> and 14 to 28 days<sup>34</sup> before supplementing fat grafts but the volume ratio was not reported.<sup>34,109</sup> Only 4 studies reported the lag time between preparation of supplements to administration to the patient or the time (range) to prepare the supplements.<sup>106,108-110</sup> Three studies described the characterization of supplements; nanofat plus PRF, ASCs, cSVF.<sup>19,106,109</sup> The shared joint analyzed markers included expression of mesenchymal cell markers (CD73, CD90, and CD105) albeit that these are not restricted to mesenchyme, integrin  $\beta 1$  (CD29), and the absence of leukocyte markers (CD45).

**Table 1.** Study Characteristics

Author (year)	Design	Follow up (months)	Indication	Pathology	Injection site	Total (n)	Age (years)	Female (n)	BMI (kg/m <sup>2</sup> )	Comorbidities	Intervention (fat +)	Intervention (n)	Control	Control (n)	Minor complications	Major complications
Bashir et al 2019	C2G	6	UP	Hemifacial atrophy, craniofacial microsomia, posttraumatic and postinfective deformity	NR	37	24.9 [8.1]	28	NR	NR	cASC	16	Fat	21	"Most patients"	Both in control and intervention group: 6% cellulitis
Bernardini et al 2015	C1G	12	C + FL		Brows, upper sulcus, inferior orbit hollow, tear trough, perioral area, malar and zygomatic areas, lips, chin, temporal fossa	98	51	92	NR	NR	PRP	98	—	—	4%	3% of patients oil cyst, 1 case requiring surgical removal
Castro-Govea et al 2018	C1G	18	UP	Craniosynostosis	Forehead	12	6	8	NR	NR	cSVF	12	—	—	0	0
Cervelli et al 2009	RC	18	UP	Scars, Parry-Romberg, hemifacial atrophy, mandibular cyst	Zygomatic region, cheek, buccal rim, upper and lower eyelid, temporal area, orbital area	25	NR	NR	NR	Diabetes, hypertension, nasal polypus, neurologic disease, arteriopathy, cardiologic disease, dislipidemy, trauma	PRP	19	Fat	10	0	0
Chang et al 2013	CCT	18	UP	Hemifacial atrophy	NR	20	27.5	12	NR	—	cSVF	10	Fat	10	0	0
Fontdevila et al 2014	RCT	12	UP	HIV lipodystrophy	Cheeks	49	46.3 [7.4]	16	24.3 [3.2]	Diabetes, hypertension, hypercholesterolemia, hypertriglyceridemia, fibrates/statin/ antidepressant/ anxiolytic/ antidiabetic drug use	PRP	20	Fat	29	0	0
Gennai et al 2017	C1G	6	C + FL		Periocular, perioral area	65	49.7	58	NR	NR	PRP	65	—	—	0	0
Gentile et al 2014	C2G	12	UP	Burns, posttraumatic scars	NR	20	NR	10	NR	NR	cSVFPRP	1010	Fat	10	0	0
Gentile et al 2020	C2G	60	C		Zygomatic/ cheek region, lower orbital area, nasolabial fold, lips	63	42.1 <sup>d</sup>	63	27 (21-33.16)	—	tSVF	33	Fat	30	Intervention group: 9%; control group: 13%	0
Gu et al 2018	C1G	6	UP	Scars	NR	20 (25 scars)	38.3	14	NR	—	tSVF	25	—	—	NR	NR
Hesamirostami et al 2019	C1G	30	C		Forehead	56	40.2	52	NR	NR	PRP	56	—	—	0	0
Jianhui et al 2014	C2G	12	UP	Parry-Romberg	NR	36	24.3 [6.6] <sup>d</sup>	25	NR	NR	Intra-operative BMSC	10	Fat	26	0	0

Table 1. Continued

Author (year)	Design	Follow up (months)	Indication	Pathology	Injection site	Total (n)	Age (years)	Female (n)	BMI (kg/m <sup>2</sup> )	Comorbidities	Intervention (fat +)	Intervention (n)	Control (n)	Control (n)	Minor complications	Major complications
Keyhan et al 2013	RCT <sup>c</sup>	12	C		Cheek, cheekbone area	25	45	17	NR	—	PRP	25 <sup>c</sup>	Fat/PRF	25 <sup>c</sup>	0	0
Koh et al 2012	CCT	15	UP	Parry-Romberg	NR	10	28	5	NR	—	cASC	5	Fat	5	0	0
Lee et al 2012	C1G <sup>c</sup>	11	C + FL		Malar eminence, infraorbital region, nasolabial fold	9	43.3	6	NR	NR	cSVF	9 <sup>c</sup>	Fat	9 <sup>c</sup>	0	0
Li et al 2013	C2G	6	NRG		Temporal, cheek, facial asymmetry	38	29.4 [6.6] <sup>d</sup>	38	NR	NR	cSVF	26	Fat	12	"Most patients"	0
Ozer et al 2019	C1G	9	C		NR	14	44.9 [11.9]	14	NR	NR	PRP	14	—	—	0	0
Sasaki et al 2015	C2G	12	C + FL		Midface	236	61.5 <sup>d</sup>	227	22.2 (16.9–32.3) <sup>d</sup>	—	PRP cSVF cSVF/PRP	106 929	Fat	92	"All patients"	0
Sasaki et al 2019	RCT <sup>c</sup>	12	C + FL		Midface	10	54.4	10	22.4 (20.5–24.6)	—	PRP	10 <sup>c</sup>	Fat/saline	10 <sup>c</sup>	"All patients"	0
Schendel et al 2015	C1G	17	C		Temples, malar areas, forehead/ glabella, eyelid area, lips, chin	10	51.6 [9.6]	10	NR	NR	cSVF	10	—	—	0	0
Sterodimas et al 2011	CCT	18	UP	Several congenital or acquired facial tissue defects	NR	20	45.1 <sup>d</sup>	10	21.6 <sup>d</sup>	Smoking, hypertension, diabetes, COPD	cSVF	10	Fat	10	"Most patients"	Control group: 10% infection
Tanikawa et al 2013	RCT	6	UP	Craniofacial microsomia	NR	14	15.4 [5.6] <sup>d</sup>	9	<25	NR	cSVF	7	Fat	7	"All patients"	0
Tenna 2017	CCT	6	UP	Acne scars	Cheeks	30	NR	NR	NR	—	Fat/PRP/ laser	15	Fat/PRP	15	NR	NR
Wei et al 2017	CCT	24	C		Tempora, geisoma, frontal part, palpebra sup inf, lacrimal groove, zygoma, cheeks, nasolabial groove, chin, marionette lines, submaxilla	139	28.5	NR	NR	NR	Nanofat/PRF	62	Fat	77	0	0
Willemsen et al 2018	RCT	12	C		Temporal, midface, nasolabial fold, marionette lines, prejowling, chin	25	52.1 [6.8]	32	(20–25)	NR	PRP	13	Fat/saline	12	0	0
Yin et al 2020	RCT	50	C		Forehead, temporal, cheek/ zygomatic, nasolabial fold	50	35.4 [8.2] <sup>d</sup>	50	21.4 [1.9] <sup>d</sup>	—	cSVF	25	Fat	25	0	0



Table 1. Continued

Author (year)	Design	Follow up (months)	Indication	Pathology <sup>a</sup>	Injection site	Total (n)	Age (years)	Female (n)	BMI (kg/m <sup>2</sup> )	Comorbidities	Intervention (fat +)	Intervention (n)	Control	Control (n)	Minor complications	Major complications
Yoshimura et al 2008	CCT	13	UP	Parry-Romberg and lupus lipomatrophy	NR	6	42.5 [8.0] <sup>d</sup>	4	NR	NR	cSVF	3	Fat	3	"All patients"	Control group: 33% necrotized tissue requiring surgical removal

Where indicated, values are mean [standard deviation] or mean (range); NR, not reported; COPD, chronic obstructive pulmonary disease. Study design: RCT, randomized controlled trial; CCT, controlled clinical trial; Cohort 2G, cohort study (2 groups, pre- + postoperative); Cohort 1G, cohort study (1 group pre- + postoperative); Retrospective, retrospective study. Indication: UP, underlying pathology, meaning with underlying disease, trauma, or congenital volume loss; C, cosmetic, meaning with no underlying pathology or facial disease, such as fat grafting for facial rejuvenation; C + FL, cosmetic with concomitant facelift. Enrichments, PRP, platelet-rich plasma; PRF, platelet-rich fibrin; cSVF, cellular stromal vascular fraction; tSVF, tissue stromal vascular fraction; cASC, cultured adipose-derived stromal cell; BMSC, bone marrow–derived stromal cell. <sup>a</sup>In the cosmetic group, there is no pathology present (ie, facial rejuvenation). <sup>b</sup>When decimals are reported, these are rounded to 1 decimal place. <sup>c</sup>Split-face design: in the studies using a split-face design: the patients themselves serve as both intervention group (one half of the face) and control group (the other half of the face). <sup>d</sup>When data are presented per group, the pooled value is calculated. —, not present in the study reported (eg, no control group was present or no complications occurred in the study).

Influence of Supplementation Therapies on Fat Graft Retention

Twenty studies assessed volume retention of supplemented fat grafts after 3 to 36 months, of which 3 studies reported multiple supplementation groups (PRP/cSVF, PRP/cSVF/PRP + cSVF, PRP/tSVF).<sup>102-104</sup> Volume was measured by computed tomography (CT), MRI, 3-dimensional (3D) surface imaging, ultrasound, visual 2D photograph assessment, numeric rating scale (NRS), or Likert scale. Seven studies used 3D surface imaging to assess fat graft retention. Volume measurement methods were often not validated and details of volumetric measurements were often not described, or described too briefly to allow for reproduction of studies.

Out of the 9 studies in which the graft was supplemented with PRP, 2 showed a difference between groups.<sup>103,120</sup> One study showed a 30% increase of volume compared to the control, ie, conventional fat grafting.<sup>103</sup> The other study showed a difference of 5% less retention in the PRP group compared to the control group, in which PRF was used as a control.<sup>120</sup> In 4 out of 9 PRP studies there was no difference between groups.<sup>99,101,105,111</sup> In the other 3 studies no statistical tests were performed or could not be performed due to the absence of controls.<sup>45,104,114</sup>

The 2 studies investigating supplementation of culture-expanded ASCs both showed a difference when compared with the conventional fat graft.<sup>34,109</sup> The volume retention varied from 1.5-fold higher<sup>109</sup> to 3-fold higher.<sup>34</sup> Seven out of 9 studies with cSVF as supplement showed a statistically significant increased volume compared with the conventional fat graft (1.2- to 1.9-fold).<sup>97,103,104,106-108,119</sup> Two studies showed no increased volume. One study

without a control group reported a retention of 68%.<sup>100</sup> In 1 study no difference between groups was found. Only 6 patients were included in that study and surgeons assessed volume visually from 2D photographs.<sup>4</sup>

One study investigating tSVF supplementation showed improved outcomes.<sup>112</sup> A 2-fold increase in volume in the supplemented group was found, but the measurement methods on MRI were not described.<sup>112</sup> The only study describing PRP and cSVF mixed as a supplement showed significantly increased volume retention (70%).<sup>103</sup> However, the mix of PRP and cSVF did not result in additional volume increase compared with cSVF (73%) or PRP (69%) alone.

Influence of Supplementation Therapies on Patient Satisfaction

Patient satisfaction or patient-reported outcome measures (PROMs) are considered the key outcome measurement of facial aesthetic procedures.<sup>121</sup> Validated and reliable outcome measures, eg, the FACE-Q questionnaire, are readily available.<sup>122,123</sup> Sixteen studies assessed patient satisfaction with the FACE-Q, the Patient and Observer Assessment Scale (POSAS), the Global Aesthetic Improvement Scale (GAIS), a visual analog scale (VAS), the Likert scale, or an NRS. The FACE-Q, GAIS, and POSAS are the only validated outcome measures and were used in 4 studies only.

To evaluate the differences in patient satisfaction between procedures in a controlled trial, the satisfaction for both the intervention and the control group should be evaluated and statistically tested for differences. Nine studies performed these “between-group” comparisons,

**Table 2.** Volume Outcomes

Author (year)	Outcome assessment	Follow up (months)	Intervention % retention	Control % retention	Fold change	Difference in retention (intervention compared with control)
PRP/PRF						
Bernardini et al 2015	VA of volume	6	Good result (63%), excellent result (37%)	—		—
Cervelli et al 2009	VA of volume	18	65%	26%	2.5	—
Fontdevila et al 2014	CT	12	NR	NR		−0.3 mL (−1.1 to −0.5 mL) <sup>a</sup> (NS)
Gentile et al 2014	MRI	12	69%	39%	1.8	—
Keyhan et al 2013	Linear measurements of photographs	12	82% (PRP)	87% (PRF)	ND	5% ↑ (PRF) ( $P < 0.05$ )
Sasaki et al 2015	3D SI	12	69% [40%]	38% [13%]	1.8	31% ↑ ( $P < 0.01$ )
Sasaki et al 2019	3D SI	12	24% [10%]	21% [1%]	1.1	3% ↑ NS
Tenna et al	US	12	0.7 cm improvement	0.6 cm improvement	1.1	0.1 cm ↑ NS
Willemssen et al 2018	VA of nasolabial fold	12	NR	NR	ND	NS
ASCs						
Bashir et al 2019	US	6	95% [4%]	31% [13%]	3.1	64% ↑ ( $P < 0.001$ )
Koh et al 2012	3D SI	6	79%	53%	1.5	26% ↑ ( $P = 0.002$ )
cSVF						
Chang et al 2013	CT	6	68% [2%]	59% [1%]	1.2	10% ↑ ( $P < 0.001$ )
Gentile et al 2014	MRI	12	63%	39%	1.6	24% ↑ ( $P < 0.0001$ )
Lee et al 2012	NRS (1-10)	3	Malar eminence 7 (6-8) Infraorbital region 7 (6-9) Nasolabial fold 8 (7-9) <sup>c</sup>	Malar eminence 6 (5-7) Infraorbital region 6 (5-6) Nasolabial fold 6 (5-8) <sup>c</sup>	Malar 1.2 Infraorbital 1.2 Nasolabial 1.3	Malar eminence 1 ↑ ( $P = 0.015$ ) Infraorbital region 1 ↑ ( $P = 0.010$ ) Nasolabial fold 2 ↑ ( $P = 0.017$ )
Li et al 2013	CT	6	65% [10%]	46% [9%]	1.4	18% ↑ ( $P < 0.01$ )
Sasaki et al 2015	3D SI	12	73% [50%]	38% [13%]	1.9	35% ↑ ( $P < 0.01$ )
Schendel et al 2015	3D SI	12	68%	—	ND	—
Tanikawa et al 2013	CT	6	88% [13%]	54% [20%]	1.6	34% ↑ ( $P = 0.002$ )
Yin et al 2020	3D SI (handheld)	6	78% [12%]	56% [10%]	1.4	21% ↑ ( $P < 0.001$ )
Yoshimura et al 2008	LS (1-4)	12	NR	NR	ND	NS



**Table 2.** Continued

Author (year)	Outcome assessment	Follow up (months)	Intervention % retention	Control % retention	Fold change	Difference in retention <sup>a</sup> (intervention compared with control)
tSVF						
Gentile et al 2020	MRI	36	61% [5%]	31% [5%]	2	30% ↑ ( $P < 0.0001$ )
PRP + cSVF						
Sasaki et al 2015	3D SI	12	70% [35%]	38% [13%]	1.8	31% ↑ ( $P < 0.01$ )

Where indicated, values are mean [standard deviation] or (range). —, no test was performed, or no quantification was described; NR, not reported; NS, not significant. Outcome assessment: NRS, numeric rating scale; US, ultrasound; CT, computed tomography; LS, Likert scale; VA, visual assessment; SI, surface imaging. Supplements: PRP, platelet-rich plasma; PRF, platelet-rich fibrin; cSVF, cellular stromal vascular fraction; tSVF, tissue stromal vascular fraction; ASC, adipose-derived stromal cell; BMSC, bone marrow–derived stromal cell. <sup>a</sup>Fontdevila et al described no separate intervention or control volume. Only a difference between groups with a range was described. <sup>b</sup>Difference is described in absolute percentage points; however, for the readability of this table we have used the percentage sign %. Differences are based on the original (not rounded) data, which means rounding errors can be present. <sup>c</sup>Lee et al described surgeon-rated volume consistency based on a numeric rating scale. <sup>d</sup>Gu et al described the thickness using the POSAS questionnaire. The specific question about thickness is extracted.

but only 6 of these 9 studies performed statistical testing. Patient satisfaction assessment was sometimes performed together (or in the same room) with the operating surgeon,<sup>116</sup> which may have induced interviewer bias and social desirability bias. Other studies omitted to describe the conditions under which measurements were performed and how results were obtained.<sup>102,104,112</sup> Follow up was sometimes not reported or ranged considerably within studies (3–30 months).<sup>109,112,113,118</sup>

Overall, patients reported high satisfaction rates after both conventional and supplemented facial fat grafting. Statistical tests were performed in 8 out of 16 studies.<sup>98,101,102,110–112,117,119</sup> Six of these 8 studies statistically tested for differences between the intervention and control group, of which 3 reported improved satisfaction in the intervention group.<sup>101,102,110–112,117,119</sup> Two PRP studies showed no significant improvement, of which the study of Tenna et al compared PRP with or without laser.<sup>101,111</sup> One cSVF study showed significant improvement and 1 cSVF showed no significant improvement.<sup>110,119</sup> Two tSVF studies showed significant improvement.<sup>102,112</sup>

## Complications

Minor complications occurred in 9 out of 27 studies. Three out of these 9 studies also reported major complications occurring in the acceptor site. Major complications were reported in the groups supplemented with ASCs and PRP and were also reported in the control groups (conventional fat grafting). Overall, bruising and swelling were the most common minor complications reported. Of the studies that reported major complications Bernardini et al reported 3 cases of oily cysts that required surgical removal.<sup>114</sup> Bashir et al reported 2 cases of cellulitis: 1 in the intervention and 1 in the control group.<sup>34</sup> Yoshimura et al reported a case of

necrotized tissue in the control group that was surgically removed.<sup>4</sup>

## DISCUSSION

Our study systematically reviewed the current literature to assess the efficacy of supplemented clinical facial fat grafting on volume retention. Our main results are that: (1) few studies include volumetric data or patient satisfaction; (2) these studies are heterogeneous with respect to (a) age, (b) injection frequency, (c) injection volume, (d) type of supplement, (e) mixing ratio of fat and supplement, (f) imaging, (g) concomitant interventions, (h) follow-up time, (i) outcome parameters, and (j) use of controls; and therefore (3) the low number of studies and their high heterogeneity did not allow for a proper meta-analysis.

The results showed that of all supplements, culture-derived ASCs were most effective at retaining injected fat volume, whereas addition of PRP, or mixtures of PRP and cSVF did not affect volume retention. Some of our reviewed papers assessed complications and found virtually none, irrespective of supplements. This corroborates previous studies that show fat grafting to be safe.<sup>2,124</sup>

A major shortcoming in virtually all analyzed papers is the near lack of properly described standardized procedures, and the reporting of interassay and intraassay variation. This causes several of the studies to be subjective rather than objective and unfortunately reduces the value of the outcomes.

Volume retention is the goal of facial fat grafting but is also a highly challenging parameter to measure and monitor. Several studies used validated imaging methods, including CT and MRI scanning or 3D surface imaging. It was

**Table 3.** Patient Satisfaction Outcomes

Author (publication year)	Outcome assessment	Follow up (months)	Comparison	Comparison with preoperative photographs	Satisfaction intervention	Satisfaction control	Difference in satisfaction (intervention compared with control or postoperative compared with preoperative)
PRP/PRF							
Gennai et al 2017	LS (1-4)	6	Within-group outcome	Yes	Fair to good effect (2.6)	—	—
Gentile et al 2014	LS (1-6)	12	Within-group outcome	Yes	nr	—	—
Hesamirostami et al 2019	GAIS	12 (6-30)	Within-group outcome	Yes	Moderate to excellent improvement, 7% poor improvement.	—	—
Ozer et al 2019	FACE-Q	9	Within-group change	—	Improved from 28.4 [23.3] to 90.3 [17.5]	—	61.9 † ( $P < 0.001$ )
Tenna et al 2017	FACE-Q	6	Between-group outcome	No	84% <sup>b</sup>	81% <sup>b</sup>	NS
Willemsen et al 2018	VAS (1-10)	6	Between-group outcome	No	NR	NR	NS
ASCs/BMSCs							
Bashir et al 2019	LS (1-5)	6	Between-group outcome	Yes	4.3 [0.7]	2.5 [0.5]	1.8 † NSR
Jianhui et al	LS (1-3)	NR	Between-group outcome	No	NR	NR	—
Koh et al 2012	VAS (1-5)	NR	Between-group outcome	No	4.5	3.1	1.4 † NSR
cSVF							
Castro-Govea et al 2018	LS of parents (1-5)	18	Within-group outcome	No	67% of the parents were satisfied and 33% were slightly satisfied	—	—
Lee et al 2012	NRS (1-10)	3	Between-group outcome	Yes	Malar eminence 7 (6-8) Infraorbital fold 8 (7-9) Nasolabial fold 8 (7-9) <sup>a</sup>	Malar eminence 6 (5-8) Infraorbital fold 6 (5-7) Nasolabial fold 7 (5-8) <sup>a</sup>	Malar eminence 1 † ( $P = 0.008$ ) Infraorbital fold 2 † ( $P = 0.010$ ) Nasolabial fold 1 † ( $P = 0.011$ )
Sterodimas et al 2011	LS (1-5)	18	Between-group outcome	No	4.0 <sup>b</sup>	4.0 <sup>b</sup>	0 NS
Yin et al 2020	LS (1-5)	6	NR	No	—	—	—
tSVF							
Gentile et al 2020	LS (1-6)	NR	Between-group outcome	No	91% fully satisfied and 9% not fully satisfied	37% fully satisfied and 63% not fully satisfied	( $P = 0.031$ )
Gu et al 2018	POSAS	12	Within-group change	Yes	Preoperative 28.8 [1.0] vs postoperative 12.2 [0.8]	—	16.6 † ( $P < 0.001$ ) <sup>d</sup>

Table 3. Continued

Author (publication year)	Outcome assessment	Follow up (months)	Comparison	Comparison with preoperative photographs	Satisfaction intervention	Satisfaction control	Difference in satisfaction (intervention compared with control or postoperative compared with preoperative)
Wei et al 2017	nr	24	Between group outcome	No	90%	70%	20% ↑ ( <i>P</i> < 0.01)

Where indicated, values are mean [standard deviation] or (range). NR, not reported; NS, not significant; NSR, no significance reported, no statistical test was performed/reported; —, no quantification, no intervention or control group present or no statistical test reported. Outcome assessment: NRS, numeric rating scale, with a higher number meaning a better score; LS, Likert scale, each number represents an outcome, such as unsatisfactory-slightly satisfactory, satisfactory; VAS, visual analog scale; FACE-Q, a validated questionnaire using a combination of Likert scales and visual analog scales; POSAS, a validated questionnaire specifically designed for scars (the overall patient-reported POSAS score is reported in this table; a lower score means a greater satisfaction); GAIS, Global Aesthetic Improvement Scale is a Likert scale, 0-4. Supplements: PRP, platelet-rich plasma; PRF, platelet-rich fibrin; cSVF, cellular stromal vascular fraction; tSVF, tissue stromal vascular fraction; ASC, adipose-derived stromal cell; BMSC, bone marrow-derived stromal cell. <sup>a</sup>Overall patient satisfaction was noted from the patient satisfaction scores. <sup>b</sup>Data were manually calculated from the tables in the article. <sup>c</sup>Within-group outcome means that no comparison to baseline or comparison to a control group was made. Participants were asked to evaluate the outcome after surgery without evaluating the preoperative situation. <sup>d</sup>A lower score of the POSAS questionnaire means a greater satisfaction.

surprising to note that none of the papers disclosed the unbiased reliability, ie, inter- and intrameasurement variation, as well as inter- and intraobserver variation. This reduces the value of the measurements as these are prone to subjective bias.

With regard to the use of validated inquiries to measure patient satisfaction and outcome, the FACE-Q, GAIS, and POSAS have been available for several years.<sup>121-123</sup> Unfortunately, no more than a quarter of the papers report utilizing these instruments. Again, comparisons with these instruments were not reported, but we included these in our results. In general, statistical testing of outcomes was neglected in more than half of the studies. We consider this a major flaw that reduces the value of potentially relevant clinical trials to a minimum. Journal editorial boards and peer-review processes should continue to improve their standards for statistics.

Our quest was to find published papers that reported the benefit of supplemented fat grafting on volume retention. However, we could neither corroborate nor dispute these findings based on our current systematic literature analyses on supplemented clinical facial fat grafting. This study focused on supplemented fat grafting in the facial area, which might be a strength or a limitation. A systematic review on fat graft supplementation in other body parts would be interesting because it may elucidate whether supplementation therapies are effective and the influence of body location on fat graft viability. One Russian study was excluded because no translation was available in the medical library. However, it is doubtful whether inclusion of this study would have changed the general message of this systematic review. Future studies should focus on conducting well-designed randomized controlled clinical

trials to be able to establish a higher level of evidence and to minimize inter- and intrastudy variation. Volume outcome measurement should be performed with valid imaging modalities and reliable volume measurement methods. Inter- and intrameasurement variation should be measured and reported. Imaging modalities based on ionizing radiation, such as CT, for follow up should be avoided. Validated patient-reported outcome questionnaires should be used and recorded both pre- and postoperatively to minimize potential recall bias. Procedures for harvesting and processing should be standardized.<sup>12,125,126</sup> No concomitant procedures such as a facelift or blepharoplasty should be performed during these studies because these influence volume outcome and patient satisfaction. We have established a summary of recommendations for the design of future trials in Table 5.

CONCLUSIONS

Despite multiple studies showing improved volume retention and increased patient satisfaction, no clinical superiority of supplementations could be objectified. Future well-designed clinical trials may elucidate whether supplementation therapies enhance fat graft retention and may increase patient satisfaction.

Supplemental Material

This article contains supplemental material located online at [www.aestheticsurgeryjournal.com](http://www.aestheticsurgeryjournal.com).

Acknowledgments

Drs Schipper and Vriend made an equal contribution to this work as co-first authors.

**Table 4.** Quality of the Included Studies Based on the Effective Public Health Practice Project Tool

Reference	Selection bias	Study Design	Confounders	Blinding	Data Collection	Dropouts	Global rating
Bashir et al 2019	0	0	–	0	+	–	–
Bernardini et al 2015	–	0	–	0	–	–	–
Castro-Govea et al 2018	–	0	–	0	–	–	–
Cervelli et al 2009	–	0	–	–	–	–	–
Chang et al 2013	–	+	–	0	–	–	–
Fontdevila et al 2014	0	+	+	+	–	+	0
Gennai et al 2017	–	0	–	–	–	NA	–
Gentile et al 2014	–	0	+	0	0	–	–
Gentile et al 2020	–	0	–	–	0	–	–
Gu et al 2018	–	0	–	–	+	–	–
Hesamirostami et al 2019	0	0	–	–	+	+	–
Jianhui et al 2014	–	0	–	–	–	–	–
Keyhan et al 2013	–	+	+	0	–	–	–
Koh et al 2012	–	+	+	0	+	–	–
Lee et al 2012	–	0	+	0	–	–	–
Li et al 2013	–	0	+	0	0	NA	0
Ozer et al 2019	–	0	+	0	+	NA	0
Sasaki et al 2015	–	0	–	–	0	–	–
Sasaki et al 2019	–	+	+	0	0	–	–
Schendel et al 2015	–	0	+	0	0	+	0
Sterodimas et al 2011	–	+	0	0	–	–	–
Tanikawa et al 2013	0	+	+	0	0	0	+
Tenna et al 2017	–	+	–	0	+	–	–
Wei et al 2017	–	+	–	0	–	–	–
Willemssen et al 2018	–	+	+	0	+	0	0
Yin et al 2020	–	+	+	+	0	+	0
Yoshimura et al 2008	–	+	+	0	–	–	–
Totals							
Weak, n (%)	23 (85%)	0 (0%)	13 (48%)	7 (26%)	12 (44%)	18 (67%)	20 (74%)
Moderate, n (%)	4 (15%)	15 (56%)	1 (4%)	18 (67%)	8 (30%)	2 (7%)	6 (22%)
Strong, n (%)	0 (0%)	12 (44%)	13 (48%)	2 (7%)	7 (26%)	4 (15%)	1 (4%)

The totals at the bottom represent the distribution of how weak, moderate and strong each criterion is. Ref, reference, +, strong, 0, moderate, –, weak.

## Disclosures

The authors declared no potential conflicts of interest with respect to the research, authorship, and publication of this article.

## Funding

This study was funded by the Departments of Oral and Maxillofacial Surgery, Plastic and Reconstructive Surgery, and

**Table 5.** Recommendations for the Study Design of New Trials

Recommendations for new studies	
Quality of the study	1. Controlled design (comparison with standard treatment or placebo) 2. Randomized 3. Minimal follow-up duration of 12 months 4. Following CONSORT <sup>a</sup> statement for reporting 5. Statistically testing for differences between groups
Standardization of the procedure	1. Standardized harvesting, processing and injection technique 2. Standardized injection volume and volume-to-volume ratio of supplement-to-fat graft 3. No concomitant procedures (eg, facelift) that can influence volume or satisfaction outcomes 4. Single injections, no repeated procedures
Measurement of volume retention	1. Clear definition of how retention is measured, based on injected volume or based on first volume measurement after surgery 2. Using valid imaging modalities (without ionizing radiation) 3. Using a reliable method of volume measurement, by either reporting reliability or using a validated method of volume measurement
Measurement of patient satisfaction	1. Using a validated PROM <sup>b</sup> 2. Measuring change of PROM, including a preoperative (baseline) measurement 3. Statistically testing for difference of PROM between intervention and control group 4. Observer/surgeon should not be present when PROM is recorded, to exclude interviewer/social desirability bias

<sup>a</sup>Consolidated Standards of Reporting Trials. <sup>b</sup>Patient-reported outcome measures.

Pathology and Medical Biology, University and Medical Center Groningen, Groningen, the Netherlands.

## REFERENCES

1. Neuber F. Verhandlungen der Deutschen Gesellschaft für Chirurgie. 1893;1:66.
2. Krastev TK, Beugels J, Hommes J, et al. Efficacy and safety of autologous fat transfer in facial reconstructive surgery: a systematic review and meta-analysis. *JAMA Facial Plast Surg*. 2018;20(5):351-360. doi: [10.1001/jamafacial.2018.0102](https://doi.org/10.1001/jamafacial.2018.0102)
3. Køllef FT, Fischer-Nielsen A, Mathiasen AB, et al. Enrichment of autologous fat grafts with ex-vivo expanded adipose tissue-derived stem cells for graft survival: a randomised placebo-controlled trial. *Lancet*. 2013;382(9898):1113-1120. doi: [10.1016/S0140-6736\(13\)61410-5](https://doi.org/10.1016/S0140-6736(13)61410-5)
4. Yoshimura K, Sato K, Aoi N, Kurita M. Cell-assisted lipotransfer for facial lipoatrophy: efficacy of clinical use of adipose-derived stem cells. *Dermatol Surg*. 2008;34:1178-85. doi: [10.1111/j.1524-4725.2008.34256.x](https://doi.org/10.1111/j.1524-4725.2008.34256.x)
5. Lv Q, Li X, Qi Y, et al. Volume retention after facial fat grafting and relevant factors: a systematic review and meta-analysis. *Aesthetic Plast Surg*. 2021;45(2):506-520. doi: [10.1007/s00266-020-01612-6](https://doi.org/10.1007/s00266-020-01612-6)
6. Ye RZ, Richard G, Gévry N, et al. Fat cell size: measurement methods, pathophysiological origins, and relationships with metabolic dysregulations. *Endocr Rev*. 2022;43(1):35-60. doi: [10.1210/edrev/bnab018](https://doi.org/10.1210/edrev/bnab018)
7. Eto H, Kato H, Suga H, et al. The fate of adipocytes after nonvascularized fat grafting: evidence of early death and replacement of adipocytes. *Plast Reconstr Surg*. 2012;129(5):1081-1092. doi: [10.1097/PRS.0b013e31824a2b19](https://doi.org/10.1097/PRS.0b013e31824a2b19)
8. Maclean PS, Higgins JA, Giles ED, et al. The role for adipose tissue in weight regain after weight loss. *Obes Rev*. 2015;16(Suppl 1):45-54. doi: [10.1111/obr.12255](https://doi.org/10.1111/obr.12255)
9. Serra-Mestre JM, Serra-Renom JM, Martinez L, et al. Platelet-rich plasma mixed-fat grafting: a reasonable pro-survival strategy for fat grafts? *Aesthetic Plast Surg*. 2014;38(5):1041-1049. doi: [10.1007/s00266-014-0374-7](https://doi.org/10.1007/s00266-014-0374-7)
10. Smith OJ, Kanapathy M, Khajuria A, et al. Protocol for a systematic review of the efficacy of fat grafting and platelet-rich plasma for wound healing. *Syst Rev*. 2017;6(1):111. doi: [10.1186/s13643-017-0505-8](https://doi.org/10.1186/s13643-017-0505-8)
11. Luck J, Smith OJ, Mosahebi A. A systematic review of autologous platelet-rich plasma and fat graft preparation methods. *Plast Reconstr Surg Glob Open*. 2017;5(12):1-14. doi: [10.1097/GOX.0000000000001596](https://doi.org/10.1097/GOX.0000000000001596)
12. Tuin AJ, Dommers PN, Schepers RH, et al. What is the current optimal fat grafting processing technique? A systematic review. *J Cranio-Maxillofacial Surg*. 2016;44(1):45-55. doi: [10.1016/j.jcms.2015.10.021](https://doi.org/10.1016/j.jcms.2015.10.021)
13. van Dongen JA, Tuin AJ, Spiekman M, et al. Comparison of intraoperative procedures for isolation of clinical grade stromal vascular fraction for regenerative purposes: a systematic review. *J Tissue Eng Regen Med*. 2018;12(1):e261-e274. doi: [10.1002/term.2407](https://doi.org/10.1002/term.2407)
14. Tonnard P, Verpaale A, Carvas M. Fat grafting for facial rejuvenation with nanofat grafts. *Clin Plast Surg*. 2020;47(1):53-62. doi: [10.1016/j.cps.2019.08.006](https://doi.org/10.1016/j.cps.2019.08.006)
15. Rihani J. Microfat and nanofat: when and where these treatments work. *Facial Plast Surg Clin North Am*. 2019;27(3):321-330. doi: [10.1016/j.fsc.2019.03.004](https://doi.org/10.1016/j.fsc.2019.03.004)
16. van Dongen JA, Tuin AJ, Harmsen MC, et al. The difference between stromal vascular fraction isolation and fat emulsification: a crucial role for centrifugation. *Plast Reconstr Surg*. 2020;145(1):232e-233e.

17. Guo J, Nguyen A, Banyard DA, et al. Stromal vascular fraction: a regenerative reality? Part 2: mechanisms of regenerative action. *J Plast Reconstr Aesthetic Surg.* 2016;69(2):180-188. doi: [10.1016/j.bjps.2015.10.014](https://doi.org/10.1016/j.bjps.2015.10.014)
18. Suga H, Glotzbach JP, Sorkin M, et al. Paracrine mechanism of angiogenesis in adipose-derived stem cell transplantation. *Ann Plast Surg.* 2014;72(2):234-241. doi: [10.1097/SAP.0b013e318264fd6a](https://doi.org/10.1097/SAP.0b013e318264fd6a)
19. Cai W, Yu LD, Tang X, Shen G. The stromal vascular fraction improves maintenance of the fat graft volume: a systematic review. *Ann Plast Surg.* 2018;81(3):367-371. doi: [10.1097/SAP.0000000000001589](https://doi.org/10.1097/SAP.0000000000001589)
20. Matsumoto D, Sato K, Gonda K, et al. Cell-assisted lipotransfer: supportive use of human adipose-derived cells for soft tissue augmentation with lipoinjection. *Tissue Eng.* 2006;12(12):3375-3382. doi: [10.1089/ten.2006.12.3375](https://doi.org/10.1089/ten.2006.12.3375)
21. Eisenstein M. Regulation: rewriting the regenerative rulebook. *Nature.* 2016;540(7632):S64-S67. doi: [10.1038/540S63a](https://doi.org/10.1038/540S63a)
22. van Dongen JA, Stevens HP, Parvizi M, et al. The fractionation of adipose tissue procedure to obtain stromal vascular fractions for regenerative purposes. *Wound Repair Regen.* 2016;24(6):994-1003. doi: [10.1111/wrr.12482](https://doi.org/10.1111/wrr.12482)
23. Yao Y, Cai J, Zhang P, et al. Adipose stromal vascular fraction gel grafting: a new method for tissue volumization and rejuvenation. *Dermatol Surg.* 2018;44(10):1278-1286. doi: [10.1097/dss.0000000000001556](https://doi.org/10.1097/dss.0000000000001556)
24. Dohan Ehrenfest DM, Rasmusson L, Albrektsson T. Classification of platelet concentrates: from pure platelet-rich plasma (P-PRP) to leucocyte- and platelet-rich fibrin (L-PRF). *Trends Biotechnol.* 2009;27(3):158-167. doi: [10.1016/j.tibtech.2008.11.009](https://doi.org/10.1016/j.tibtech.2008.11.009)
25. Xiong S, Yi C, Pu LLQ. An overview of principles and new techniques for facial fat grafting. *Clin Plast Surg.* 2020;47(1):7-17. doi: [10.1016/j.cps.2019.08.001](https://doi.org/10.1016/j.cps.2019.08.001)
26. Vyas KS, Vasconez HC, Morrison S, et al. Fat graft enrichment strategies: a systematic review. *Plast Reconstr Surg.* 2020;145(3):827-841. doi: [10.1097/PRS.0000000000006557](https://doi.org/10.1097/PRS.0000000000006557)
27. Trojahn K lle S-FF, Oliveri RS, Glovinski PV, et al. Importance of mesenchymal stem cells in autologous fat grafting: a systematic review of existing studies. *J Plast Surg Hand Surg.* 2012;46(2):59-68. doi: [10.3109/2000656X.2012.668326](https://doi.org/10.3109/2000656X.2012.668326)
28. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *J Clin Epidemiol.* 2009;62(10):1006-1012. doi: [10.1016/j.jclinepi.2009.06.005](https://doi.org/10.1016/j.jclinepi.2009.06.005)
29. Schardt C, Adams MB, Owens T, et al. Utilization of the PICO framework to improve searching PubMed for clinical questions. *BMC Med Inform Decis Mak.* 2007;7:16. doi: [10.1186/1472-6947-7-16](https://doi.org/10.1186/1472-6947-7-16)
30. Jackson N, Waters E. Criteria for the systematic review of health promotion and public health interventions. *Health Promot Int.* 2005;20(4):367-374. doi: [10.1093/heapro/dai022](https://doi.org/10.1093/heapro/dai022)
31. Almadori A, Griffin M, Ryan CM, et al. Stem cell enriched lipotransfer reverses the effects of fibrosis in systemic sclerosis. *PLoS ONE.* 2019;14(7):e0218068. doi: [10.1371/journal.pone.0218068](https://doi.org/10.1371/journal.pone.0218068)
32. Amar RE, Fox DM. The facial autologous muscular injection (FAMI) procedure: an anatomically targeted deep multiplane autologous fat-grafting technique using principles of facial fat injection. *Aesthetic Plast Surg.* 2011;35(4):502-510. doi: [10.1007/s00266-010-9645-0](https://doi.org/10.1007/s00266-010-9645-0)
33. Bae YC, Park TS, Kang GB, et al. Usefulness of microfat grafting in patients with repaired cleft lip. *J Craniofac Surg.* 2016;27(7):1722-1726.
34. Bashir MM, Sohail M, Ahmad FJ, et al. Preenrichment with adipose tissue-derived stem cells improves fat graft retention in patients with contour deformities of the face. *Stem Cells Intl.* 2019;2019:5146594. doi: [10.1155/2019/5146594](https://doi.org/10.1155/2019/5146594)
35. Bhooshan LS, Geetha Devi M, Aniraj R, et al. Autologous emulsified fat injection for rejuvenation of scars: a prospective observational study. *Indian J Plast Surg.* 2018;51(1):77-83. doi: [10.4103/ijps.IJPS\\_86\\_17](https://doi.org/10.4103/ijps.IJPS_86_17)
36. Onesti MG, Fioramonti P, Carella S, et al. Improvement of mouth functional disability in systemic sclerosis patients over one year in a trial of fat transplantation versus adipose-derived stromal cells. *Stem Cells Intl.* 2016;2016:2416192. doi: [10.1155/2016/2416192](https://doi.org/10.1155/2016/2416192)
37. Virzi F, Bianca P, Giammona A, et al. Combined platelet-rich plasma and lipofilling treatment provides great improvement in facial skin-induced lesion regeneration for scleroderma patients. *Stem Cell Res Ther.* 2017;8(1):236. doi: [10.1186/s13287-017-0690-3](https://doi.org/10.1186/s13287-017-0690-3)
38. Gontijo-de-Amorim NF, Charles-de-S  L. Fat grafting for facial contouring using mechanically stromal vascular fraction-enriched lipotransfer. *Clin Plast.* 2019;47(1):99-109. doi: [10.1016/j.cps.2019.08.012](https://doi.org/10.1016/j.cps.2019.08.012)
39. Charles-de-S  L, Gontijo-de-Amorim N, Sbarbati A, et al. Photoaging skin therapy with PRP and ADSC: a comparative study. *Stem Cells Int.* 2020;2020:2032359. doi: [10.1155/2020/2032359](https://doi.org/10.1155/2020/2032359)
40. Aronowitz JA, Lockhart RA, Hakakian CS, Hicok KC. Clinical safety of stromal vascular fraction separation at the point of care. *Ann Plast Surg.* 2015;75(6):666-71. doi: [10.1097/sap.0000000000000594](https://doi.org/10.1097/sap.0000000000000594)
41. Braccini F, Chignon-Sicard B, Volpei C, Choukroun J. Modern lipostructure: the use of platelet rich fibrin (PRF). *Rev Laryngol Otol Rhinol.* 2013;134(4-5):231-235.
42. Castro-Govea Y, Garza-Pineda OL, Lara-Arias J, et al. Cell-assisted lipotransfer for the treatment of Parry-Romberg syndrome. *Arch Plast Surg.* 2012;39(6):659-662. doi: [10.5999/aps.2012.39.6.659](https://doi.org/10.5999/aps.2012.39.6.659)
43. Cervelli V, Nicoli F, Spallone D. Treatment of traumatic scars using fat grafts mixed with platelet-rich plasma, and resurfacing of skin with the 1540 nm nonablative laser. *Clin Exp Dermatol.* 2012;37(1):55-61. doi: [10.1111/j.1365-2230.2011.04199.x](https://doi.org/10.1111/j.1365-2230.2011.04199.x)
44. Cervelli V, Gentile P, Scioli MG, et al. Application of platelet-rich plasma in plastic surgery: clinical and in vitro evaluation. *Tissue Eng Part C Methods* 2009;15(4):625-634. doi: [10.1089/ten.tec.2008.0518](https://doi.org/10.1089/ten.tec.2008.0518)



45. Cervelli V, Palla L, Pascali M, et al. Autologous platelet-rich plasma mixed with purified fat graft in aesthetic plastic surgery. *Aesthet Plast Surg*. 2009;33(5):716-721. doi: [10.1007/s00266-009-9386-0](https://doi.org/10.1007/s00266-009-9386-0)
46. Charles-de-Sá L, Gontijo-de-Amorim NF, Maeda Takiya C, et al. Antiaging treatment of the facial skin by fat graft and adipose-derived stem cells. *Plast Reconstr Surg*. 2015;135(4):999-1009. doi: [10.1097/prs.0000000000001123](https://doi.org/10.1097/prs.0000000000001123)
47. Clauser L, Lucchi A, Tocco-Tussardi I, et al. Autologous fat transfer for facial augmentation and regeneration: role of mesenchymal stem cells. *Atlas Oral Maxillofac Surg Clin North Am*. 2018;26(1):25-32. doi: [10.1016/j.cxom.2017.10.002](https://doi.org/10.1016/j.cxom.2017.10.002)
48. Gontijo-de-Amorim NF, Charles-de-Sá L, Rigotti G. Fat grafting for facial contouring using mechanically stromal vascular fraction-enriched lipotransfer. *Clin Plast Surg*. 2020;47(1):99-109. doi: [10.1016/j.cps.2019.08.012](https://doi.org/10.1016/j.cps.2019.08.012)
49. Majani U, Majani A. Correction of scars by autologous fat graft and platelet rich plasma (PRP). *Acta Med Mediterr*. 2012;28:99-100.
50. Nita AC, Orzan OA, Filipescu M, Jianu D. Fat graft, laser CO<sub>2</sub> and platelet-rich-plasma synergy in scars treatment. *J Med Life*. 2013;6(4):430-433.
51. Ortega VG, Sastoque D. New and successful technique for the management of Parry-Romberg syndrome's soft tissue atrophy. *J Craniofac Surg*. 2015;26(6):e507-e510. doi: [10.1097/scs.0000000000002023](https://doi.org/10.1097/scs.0000000000002023)
52. Pallua N, Kim BS. Microfat and lipoconcentrate for the treatment of facial scars. *Clin Plast Surg*. 2020;47(1):139-145. doi: [10.1016/j.cps.2019.08.010](https://doi.org/10.1016/j.cps.2019.08.010)
53. Park KY, Kim IS, Kim BJ, Kim MN. Letter: Autologous fat grafting and platelet-rich plasma for treatment of facial contour defects. *Dermatol Surg*. 2012;38(9):1572-1574. doi: [10.1111/j.1524-4725.2012.02515.x](https://doi.org/10.1111/j.1524-4725.2012.02515.x)
54. Philandrianos C, Magalon J, Daumas A, et al. Combined PRP and microfat graft for facial disability in systemic sclerosis. *J Scleroderma Relat Disord*. 2017;2(3):7-11. doi: [10.5301/jsrd.5000261](https://doi.org/10.5301/jsrd.5000261)
55. Rigotti G, Charles-De-Sá L, Gontijo-De-Amorim NF, et al. Expanded stem cells, stromal-vascular fraction, and platelet-rich plasma enriched fat: comparing results of different facial rejuvenation approaches in a clinical trial. *Aesthet Surg J*. 2016;36(3):261-270. doi: [10.1093/asj/sjv231](https://doi.org/10.1093/asj/sjv231)
56. Tian YG, Liu XY, Tao K, et al. Adipose-derived stem cells assisted facial rejuvenation. *Chin J Tissue Eng Res*. 2013;16(49):9257-9264. doi: [10.3969/j.issn.2095-4344.2012.49.025](https://doi.org/10.3969/j.issn.2095-4344.2012.49.025)
57. Tiryaki T, Findikli N, Tiryaki D. Staged stem cell-enriched tissue (SET) injections for soft tissue augmentation in hostile recipient areas: a preliminary report. *Aesthetic Plast Surg*. 2011;35(6):965-971. doi: [10.1007/s00266-011-9716-x](https://doi.org/10.1007/s00266-011-9716-x)
58. Willemsen JC, van der Lei B, Vermeulen KM, Stevens HP. The effects of platelet-rich plasma on recovery time and aesthetic outcome in facial rejuvenation: preliminary retrospective observations. *Aesthetic Plast Surg*. 2014;38(5):1057-1063. doi: [10.1007/s00266-014-0361-z](https://doi.org/10.1007/s00266-014-0361-z)
59. Sadati KS, Corrado AC. Platelet-rich plasma (PRP) utilized to promote greater graft volume retention in autologous fat grafting. *Am J Cos Surg*. 2006;23(4):203-211. doi: [10.1177/074880680602300407](https://doi.org/10.1177/074880680602300407)
60. Abdali H, Hadilou M. Treatment of nasolabial fold with subdermal dissection and autologous fat injection added with platelet-rich plasma. *J Res Med Sci*. 2014;19(11):1110.
61. Gontijo-De-Amorim NF, Charles-De-Sá L, Rigotti G. Mechanical supplementation with the stromal vascular fraction yields improved volume retention in facial lipotransfer: a 1-year comparative study. *Aesthet Surg J*. 2017;37(9):975-985. doi: [10.1093/asj/sjx115](https://doi.org/10.1093/asj/sjx115)
62. Lee JW, Park SH, Lee SJ, et al. Clinical impact of highly condensed stromal vascular fraction injection in surgical management of depressed and contracted scars. *Aesthetic Plast Surg*. 2018;42(6):1689-1698. doi: [10.1007/s00266-018-1216-9](https://doi.org/10.1007/s00266-018-1216-9)
63. Annacontini L, Valente M, Rucci M, et al. "Cellular therapy" through lipostructuring; the role of adipose-derived adult stem cells in "regenerative surgery" processes: outcomes over the past 3 years. *Eur Surg Res*. 2010;45:238-239. doi: [10.1159/000321283](https://doi.org/10.1159/000321283)
64. Annacontini L, Parisi D, Lembo F, et al. Cellular therapy through lipostructuring; the role of adipose-derived adult stem cells in regenerative surgery processes. *J Tissue Eng Regen Med*. 2012;6(Suppl 1):268. doi: [10.1002/term.1586](https://doi.org/10.1002/term.1586)
65. Branas EB, Salvatierra BG, Torres JN, Casado-Perez C. Stromal vascular fraction- enhanced autologous fat transfer versus lipofilling in facial lipoatrophy. *Br J Surg*. 2014;101:8.
66. Castana O, Alexaki V, Pallantzas A, et al. Adipose tissue-derived mesenchymal cells for the reparation of major facial traumatic deformities. *J Invest Dermatol*. 2012;132(Suppl 2):S54. doi: [10.1038/jid.2012.298](https://doi.org/10.1038/jid.2012.298)
67. Keyhan SO. Use of platelet rich fibrin and platelet rich plasma in combination with fat graft; which is more effective during facial lipostructure? *Int J Oral Maxillofac Surg*. 2013;42(10):1252-1253. doi: [10.1016/j.ijom.2013.07.279](https://doi.org/10.1016/j.ijom.2013.07.279)
68. Lonskaya E, Kurakin K, Drobyshev A, et al. Simultaneous face fat-grafting to enhance the aesthetic outcome of orthognathic surgery. *Int J Oral Maxillofac Surg*. 2017;46(Suppl 1):162-163. doi: [10.1016/j.ijom.2017.02.558](https://doi.org/10.1016/j.ijom.2017.02.558)
69. Tamme T, Tiigimae-Saar J, Arak T. The evaluation of autologous adipose tissue grafting for facial contour deformities. *Int J Oral Maxillofac Surg*. 2019;48(Suppl 1):129. doi: [10.1016/j.ijom.2019.03.398](https://doi.org/10.1016/j.ijom.2019.03.398)
70. Chaoahua L, Chenggang Y. A clinical comparative study of volume retention rate for repairing facial depressed deformity with different operative methods of autologous fat transplantation. 2018. <https://trialsearch.who.int/Trial2.aspx?TrialID=ChiCTR1800017796>
71. Drzewiecki KT. Lipofilling with MSC enriched fat, a permanent autologous filler? 2010. <https://trialsearch.who.int/Trial2.aspx?TrialID=EUCTR2010-023006-12-DK>
72. Kamei Y, Takanari K. Augmentation of soft tissue defect in face, trunk and extremity with adipose-derived regenerative cell enriched lipotransfer. 2014. <https://trialsearch.who.int/Trial2.aspx?TrialID=JPRN-UMIN000012866>

73. Shimizu Y. Clinical study of treatment for depressed lesions using cultured adipose derived stem cells. 2016. <http://www.who.int/trialsearch/Trial2.aspx?TrialID=JPRN-UMIN000020530>
74. Kim BJ. The efficiency of stromal vascular fraction cells in facial fat graft procedures. 2018. <https://trialsearch.who.int/Trial2.aspx?TrialID=KCT0003402>
75. Choi J. The effect of human adipose tissue-derived MSCs in Romberg's disease. 2011. <https://clinicaltrials.gov/show/NCT01309061>
76. Willemsen J, Stevens J. The use of activated platelet rich plasma (PRP) in human autologous fat transfer. 2011. <https://clinicaltrials.gov/show/NCT01461785>
77. Tanikawa DY. Clinical trial of fat grafts supplemented with adipose-derived regenerative cells. 2012. <https://clinicaltrials.gov/show/NCT01674439>
78. Alonso N. Immunophenotyping of fresh stromal vascular fraction from adipose derived stem cells (ADSC) enriched fat grafts. 2013. <https://clinicaltrials.gov/show/NCT01771913>
79. Rahimian S. Adipose derived stem cells in facial fat grafting. 2015. <https://clinicaltrials.gov/show/NCT02526576>
80. Tanikawa DS. Fat grafts with adipose-derived regenerative cells for soft tissue reconstruction in children. 2019. <https://clinicaltrials.gov/show/NCT03806361>
81. Ismail A. Effect of adipose derived stem cells on survival of fat as filler. 2019. <https://clinicaltrials.gov/show/NCT03965936>
82. van Dongen J. Stromal vascular fraction (SVF) enriched lipofilling plus platelet rich plasma (PRP) for the treatment of the aging face. 2016. <https://trialsearch.who.int/Trial2.aspx?TrialID=NTR5703>
83. Herold C, Vogt PM. Radiodermatitis: with autologous stem cells enriched lipoaspirate transplantation as minimally invasive treatment option. *Haut*. 2011;22:262-265.
84. Al-Chalabi NJA, Al-Quisi AF, Abdul Lateef T. Single session facial liposuction by using autologous fat mixed with platelet-rich fibrin injected by using facial autologous muscular injection technique. *J Craniofac Surg*. 2018;29(3):e267-e271. doi: [10.1097/scs.0000000000004307](https://doi.org/10.1097/scs.0000000000004307)
85. Abuzeni PZ, Alexander RW. Enhancement of autologous fat transplantation with platelet rich plasma. *Am J Cos Surg* 2001;18(2):59-70. doi: [10.1177/074880680101800202](https://doi.org/10.1177/074880680101800202)
86. Choi JY, Lim JO. Combination of adipose-derived stem cells and oxygen microspheres for enhanced cell survival in fat transplantation. *J Tissue Eng Regen Med*. 2014;8(Suppl 1):276.
87. Modarressi A. Platelet rich plasma (PRP) improves fat grafting outcomes. *World J Plast Surg*. 2013;2(1):6-13.
88. Scalfani AP, McCormick SA. Induction of dermal collagenesis, angiogenesis, and adipogenesis in human skin by injection of platelet-rich fibrin matrix. *Arch Facial Plast Surg*. 2012;14(2):132-6. doi: [10.1001/archfacial.2011.784](https://doi.org/10.1001/archfacial.2011.784)
89. Swanson E. Does separating the stromal vascular fraction improve facial fat retention? *Plast Reconstr Surg*. 2016;137(3):637e-639e. doi: [10.1097/prs.0000000000002142](https://doi.org/10.1097/prs.0000000000002142)
90. Choudhery MS. Systemic administration of adipose-derived stromal cells concurrent with fat grafting. *Plast Reconstr Surg*. 2020;145(2):456e-457e. doi: [10.1097/prs.0000000000006451](https://doi.org/10.1097/prs.0000000000006451)
91. Kim SJ, Choi WI, Lee BI, et al. The effect of platelet-rich plasma (PRP) on the survival of the autologous fat graft. *J Korean Soc Plast Reconstr Surg*. 2007;34(3):291-297.
92. Jiang S, Quan Y, Wang J, et al. Fat grafting for facial rejuvenation using stromal vascular fraction gel injection. *Clin Plast Surg*. 2020;47(1):73-79. doi: [10.1016/j.cps.2019.09.001](https://doi.org/10.1016/j.cps.2019.09.001)
93. Nolan GS, Smith OJ, Mosahebi A. Enhancing fat graft survival with autologous growth factors: platelet-rich fibrin (PRF) vs platelet-rich plasma (PRP). *Aesthet Surg J*. 2021;41(5):NP241. doi: [10.1093/asj/sjaa274](https://doi.org/10.1093/asj/sjaa274)
94. Reksodiputro MH, Diandini D, Koento T, Arisanty R, Harahap AR. Autologous microlobular fat combined with platelet-rich fibrin is associated with good fat graft viability. *J Phys Conf Ser*. 2018;1073(3):032060. doi: [10.1088/1742-6596/1073/3/032060](https://doi.org/10.1088/1742-6596/1073/3/032060)
95. Zhao J, Yi C, Zheng Y, et al. Enhancement of fat graft survival by bone marrow-derived mesenchymal stem cell therapy. *Plast Reconstr Surg*. 2013;132(5):1149-1157. doi: [10.1097/PRS.0b013e3182a48b6c](https://doi.org/10.1097/PRS.0b013e3182a48b6c)
96. Chkadua TZ, Visaitova ZY, Strukova OO, et al. The feasibility of combined lipofilling methods in the treatment of patients with facial hemiatrophy. *Stomatol*. 2019;98(3):35-41. doi: [10.17116/stomat20199803135](https://doi.org/10.17116/stomat20199803135)
97. Li J, Gao J, Cha P, et al. Supplementing fat grafts with adipose stromal cells for cosmetic facial contouring. *Dermatologic Surg*. 2013;39(3 Pt 1):449-456. doi: [10.1111/dsu.12058](https://doi.org/10.1111/dsu.12058)
98. Ozer K, Colak O. Micro-autologous fat transplantation combined with platelet-rich plasma for facial filling and regeneration: a clinical perspective in the shadow of evidence-based medicine. *J Craniofac Surg*. 2019;30(3):672-677. doi: [10.1097/scs.0000000000005122](https://doi.org/10.1097/scs.0000000000005122)
99. Sasaki GH. A preliminary clinical trial comparing split treatments to the face and hand with autologous fat grafting and platelet-rich plasma (PRP): a 3D, IRB-approved study. *Aesthet Surg J*. 2019;39(6):675-686. doi: [10.1093/asj/sjy254](https://doi.org/10.1093/asj/sjy254)
100. Schendel SA. Enriched autologous facial fat grafts in aesthetic surgery: 3D volumetric results. *Aesthet Surg J*. 2015;35(8):913-919. doi: [10.1093/asj/sjv140](https://doi.org/10.1093/asj/sjv140)
101. Willemsen JCN, Van Dongen J, Spiekman M, et al. The addition of platelet-rich plasma to facial lipofilling: a double-blind, placebo-controlled, randomized trial. *Plast Reconstr Surg*. 2018;141(2):331-343. doi: [10.1097/prs.0000000000004081](https://doi.org/10.1097/prs.0000000000004081)
102. Wei H, Gu SX, Liang YD, et al. Nanofat-derived stem cells with platelet-rich fibrin improve facial contour remodeling and skin rejuvenation after autologous structural fat transplantation. *Oncotarget*. 2017;8(40):68542-68556. doi: [10.18632/oncotarget.19721](https://doi.org/10.18632/oncotarget.19721)
103. Sasaki GH. The safety and efficacy of cell-assisted fat grafting to traditional fat grafting in the anterior mid-face: an indirect assessment by 3D imaging. *Aesthetic Plast Surg*. 2015;39(6):833-846. doi: [10.1007/s00266-015-0533-5](https://doi.org/10.1007/s00266-015-0533-5)
104. Gentile P, Angelis B De, Pasin M, et al. Adipose-derived stromal vascular fraction cells and platelet-rich plasma: basic

- and clinical evaluation for cell-based therapies in patients with scars on the face. *J Craniofac Surg*. 2014;25(1):267-272. doi: [10.1097/01.scs.0000436746.21031.ba](https://doi.org/10.1097/01.scs.0000436746.21031.ba)
105. Fontdevila J, Guisantes E, Martinez E, et al. Double-blind clinical trial to compare autologous fat grafts versus autologous fat grafts with PDGF: no effect of PDGF. *Plast Reconstr Surg*. 2014;134(2):219E-230E. doi: [10.1097/PRS.0000000000000409](https://doi.org/10.1097/PRS.0000000000000409)
  106. Tanikawa DYS, Agüena M, Bueno DF, et al. Fat grafts supplemented with adipose-derived stromal cells in the rehabilitation of patients with craniofacial microsomia. *Plast Reconstr Surg*. 2013;132(1):141-152. doi: [10.1097/PRS.0b013e3182910a82](https://doi.org/10.1097/PRS.0b013e3182910a82)
  107. Yin Y, Li J, Li Q, et al. Autologous fat graft assisted by stromal vascular fraction improves facial skin quality: a randomized controlled trial. *J Plast Reconstr Aesthetic Surg*. 2020;73(6):1166-1173. doi: [10.1016/j.bjps.2019.11.010](https://doi.org/10.1016/j.bjps.2019.11.010)
  108. Chang Q, Li J, Dong Z, et al. Quantitative volumetric analysis of progressive hemifacial atrophy corrected using stromal vascular fraction-supplemented autologous fat grafts. *Dermatol Surg*. 2013;39(10):1465-1473. doi: [10.1111/dsu.12310](https://doi.org/10.1111/dsu.12310)
  109. Koh KS, Oh TS, Kim H, et al. Clinical application of human adipose tissue-derived mesenchymal stem cells in progressive hemifacial atrophy (Parry-Romberg disease) with microfat grafting techniques using 3-dimensional computed tomography and 3-dimensional camera. *Ann Plast Surg*. 2012;69(3):331-337.
  110. Sterodimas A, De Faria J, Nicaretta B, Boriani F. Autologous fat transplantation versus adipose-derived stem cell-enriched lipografts: a study. *Aesthet Surg J*. 2011;31(6):682-693. doi: [10.1177/1090820x11415976](https://doi.org/10.1177/1090820x11415976)
  111. Tenna S, Cogliandro A, Barone M, et al. Comparative study using autologous fat grafts plus platelet-rich plasma with or without fractional CO<sub>2</sub> laser resurfacing in treatment of acne scars: analysis of outcomes and satisfaction with FACE-Q. *Aesthetic Plast Surg*. 2017;41(3):661-666. doi: [10.1007/s00266-017-0777-3](https://doi.org/10.1007/s00266-017-0777-3)
  112. Gentile P, Sterodimas A, Calabrese C, et al. Regenerative application of stromal vascular fraction cells enhanced fat graft maintenance: clinical assessment in face rejuvenation. *Expert Opin Biol Ther*. 2020;20(12):1503-1513. doi: [10.1080/14712598.2020.1815703](https://doi.org/10.1080/14712598.2020.1815703)
  113. Jianhui Z, Chenggang Y, Binglun L, et al. Autologous fat graft and bone marrow-derived mesenchymal stem cells assisted fat graft for treatment of Parry-Romberg syndrome. *Ann Plast Surg*. 2014;73(Suppl 1):S99-S103. doi: [10.1097/sap.0000000000000238](https://doi.org/10.1097/sap.0000000000000238)
  114. Bernardini FP, Gennai A, Izzo L, et al. Superficial enhanced fluid fat injection (SEFFI) to correct volume defects and skin aging of the face and periorbital region. *Aesthetic Surg J*. 2015;35(5):504-515. doi: [10.1093/asj/sjv001](https://doi.org/10.1093/asj/sjv001)
  115. Castro-Govea Y, Vela-Martinez A, Trevino-Garcia LA. Volumetric lipoinjection of the fronto-orbital and temporal complex with adipose stem cells for the aesthetic restoration of sequelae of craniosynostosis. *Arch Plast Surg*. 2018;45(2):128-134.
  116. Gennai A, Zambelli A, Repaci E, et al. Skin rejuvenation and volume enhancement with the micro superficial enhanced fluid fat injection (M-SEFFI) for skin aging of the periorbital and perioral regions. *Aesthet Surg J*. 2017;37(1):1-10. doi: [10.1093/asj/sjw084](https://doi.org/10.1093/asj/sjw084)
  117. Gu ZC, Li YR, Li H. Use of condensed nanofat combined with fat grafts to treat atrophic scars. *JAMA Facial Plast Surg*. 2018;20(2):128-135.
  118. Hesamirostami M, Modarressi A, Lebaschi A, Kazemi Ashtiani A. Forehead biconvexity enhancement with fat grafting. *Eur J Plast Surg*. 2019;42:231-234. doi: [10.1007/s00238-018-1489-x](https://doi.org/10.1007/s00238-018-1489-x)
  119. Lee SK, Kim DW, Dhong ES, et al. Facial soft tissue augmentation using autologous fat mixed with stromal vascular fraction. *Arch Plast Surg*. 2012;39(5):534-539. doi: [10.5999/aps.2012.39.5.534](https://doi.org/10.5999/aps.2012.39.5.534)
  120. Keyhan SO, Hemmat S, Badri AA, et al. Use of platelet-rich fibrin and platelet-rich plasma in combination with fat graft: which is more effective during facial liposuction? *J Oral Maxillofac Surg*. 2013;71(3):610-621. doi: [10.1016/j.joms.2012.06.176](https://doi.org/10.1016/j.joms.2012.06.176)
  121. Cano SJ, Klassen A, Pusic AL. The science behind quality-of-life measurement: a primer for plastic surgeons. *Plast Reconstr Surg*. 2009;123(3):98e-106e. doi: [10.1097/PRS.0b013e31819565c1](https://doi.org/10.1097/PRS.0b013e31819565c1)
  122. Klassen AF, Cano SJ, Schwitzer JA, et al. Development and psychometric validation of the FACE-Q skin, lips, and facial rhytids appearance scales and adverse effects checklists for cosmetic procedures. *JAMA Dermatol*. 2016;152(4):443-451. doi: [10.1001/jamadermatol.2016.0018](https://doi.org/10.1001/jamadermatol.2016.0018)
  123. Pusic AL, Klassen AF, Scott AM, Cano SJ. Development and psychometric evaluation of the FACE-Q Satisfaction with Appearance Scale: a new patient-reported outcome instrument for facial aesthetics patients. *Clin Plast Surg*. 2013;40(2):249-260. doi: [10.1016/j.cps.2012.12.001](https://doi.org/10.1016/j.cps.2012.12.001)
  124. Zhou Y, Wang J, Li H, et al. Efficacy and safety of cell-assisted lipotransfer: a systematic review and meta-analysis. *Plast Reconstr Surg*. 2016;137(1):44e-57e. doi: [10.1097/PRS.0000000000001981](https://doi.org/10.1097/PRS.0000000000001981)
  125. Sommer B, Sattler G. Current concepts of fat graft survival: histology of aspirated adipose tissue and review of the literature. *Dermatologic Surg*. 2000;26(12):1159-1166.
  126. Gir P, Brown SA, Oni G, et al. Fat grafting: evidence-based review on autologous fat harvesting, processing, reinjection, and storage. *Plast Reconstr Surg*. 2012;130(1):249-258. doi: [10.1097/PRS.0b013e318254b4d3](https://doi.org/10.1097/PRS.0b013e318254b4d3)