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## Review

# A systematic review of the effectiveness and complications of fat grafting in the facial region<sup>☆</sup>

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## ABSTRACT

**Introduction:** The objective of this study was to evaluate the safety and efficacy of fat grafting to the facial region for the reconstruction and aesthetic enhancement of facial contour.

**Methods:** A systematic literature review of the National Library of Medicine (PubMed), MEDLINE and Cochrane databases was performed. Studies involving the outcomes of autologous fat grafting to correct or enhance contour defects of the face were included. Extracted data included patient demographics, harvest and injection sites, graft harvesting and injection technique, mean injected volume, retained volume percentage and complications.

**Results:** Forty-three articles met the inclusion criteria, resulting in 4577 patients with various facial contour defects treated with autologous fat grafting. Injection sites were categorized by anatomic facial regions as upper (32.5%), middle (53%) and lower face (14.5%). The mean volume of injected fat was 16.9 ml. The mean weighted volume retention of non-enriched grafts was 41.63% at the time of follow up (mean 13.9 months). A total of 104 (2.27%) complications were reported including asymmetry (74), skin irregularities (14), prolonged edema (4), graft hypertrophy (4), fat necrosis (3), infection (2), erythema (1), telangiectasia (1), and activation of acne (1).

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**Conclusion:** The present study represents the first systematic review of fat grafting in the facial region, a widely-performed procedure within plastic surgery practice. Importantly, it presents pooled important data such as retained grafting volume and complication rates in this anatomical region, providing clinicians with more accurate information with which to guide their decision-making and patient education.

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## Introduction

Neuber was first to describe the transfer of fat as a means of treating retractile scarring in 1893.<sup>1</sup> Fat grafting, however, has only gained widespread popularity amongst plastic surgeons over the past several decades. Its use as a treatment for both cosmetic and reconstructive contour defects has evolved due to the development of modern liposuction in the 1980's by Illouz<sup>2,3</sup> and the continued refinement of harvesting, preparation and grafting techniques such as those pioneered by Coleman.<sup>4</sup>

Fat serves as ideal soft tissue filler in that it is autologous, biocompatible, easily accessible in most patients, relatively permanent and can integrate into the surrounding tissue at the injection site.<sup>4–6</sup> The safety and effectiveness of fat grafting has been extensively studied for various indications, particularly in breast surgery for both reconstructive and cosmetic purposes.<sup>7–9</sup> Its use in the facial region has also increased, although less is published regarding its safety and effectiveness for facial reconstruction or aesthetic improvement.<sup>8,10,11</sup>

To that end, the authors have performed a systematic review of the literature, with the objective of providing more data with which to evaluate the effectiveness and associated complications of autologous fat grafting for the treatment of contour deformities in facial region.

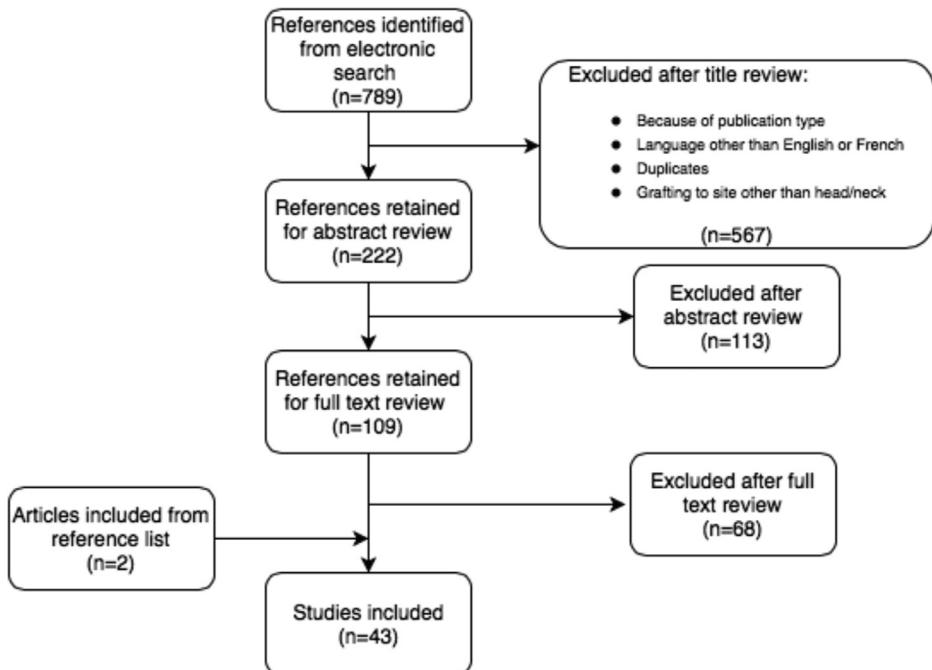
## Patients and methods

A search of the National Library of Medicine (PubMed), MEDLINE, and Cochrane databases was conducted using different versions of the following keywords: [(“fat graft” or “autologous graft” (MESH), or “adipose”) and (“graft survival” (MESH), or “complications”, or “treatment outcomes” (MESH))]. The search was confined to both English and French language articles and limited to humans. Articles from all years up until December 2015 were considered, with no restriction placed on patient age.

The resultant 789 abstracts were independently assessed by two separate reviewers according to strict inclusion and exclusion criteria. Studies were included if data regarding facial fat grafting complication rates and/or efficacy was provided. Patients receiving fat grafting as an adjunct to another therapy or dermal fat grafting were excluded in order to decrease confounding factors and to more accurately assess graft retention and complications attributed solely to fat grafting. Case reports were also excluded to limit publication bias. No limitation was placed on minimum follow up time. Forty-three full articles were retained based on our inclusion criteria of facial contour defects and the use of fat grafting as the sole treatment modality.

The selected articles were analyzed regarding patient demographics, indication for treatment, harvest site, processing technique, graft enrichment, injection site, volume injected, percentage of graft retained, follow up time and complications resulting from the procedure.

Given the large variability in the method by which injection sites were documented, cases were categorized according to anatomic facial regions treated: upper, middle, and lower. The upper third was defined as the region extending from the hairline to glabella, the middle third from glabella to subnasale and the lower third from subnasale to menton.



**Figure 1.** Flowchart of search criteria and strategy used for performance of the literature review in accordance with PRISMA guidelines.

Complications included in the analysis were erythema, prolonged edema (lasting greater than 3 weeks), telangiectasia, asymmetry, skin irregularities, graft hypertrophy, erythema, infection and fat necrosis.

The reported volume of adipose tissue retained at follow up in various studies was measured using 2-dimensional photography, 3-dimensional imaging or commuted tomography (CT) scans.

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)<sup>12</sup> (Figure 1, Table 1).<sup>6,13–54</sup>

## Results

Our search returned 789 matches, 43 of which met our inclusion criteria, representing a total of 4577 individual patients who underwent autologous fat transfer.<sup>6,13–54</sup>

### Patient demographics/characteristics

Of the 4577 included patients who underwent autologous fat transfer, 55% ( $n = 2516$ ) were female and 12.1% were male ( $n = 553$ ), with the remaining 32.9% ( $n = 1508$ ) not specified. The mean age at the time of the procedure was 36.2 years (range: 7.4–80 years) (Table 2).

The indications for treatment were clearly documented in 2040 cases. In decreasing order of prevalence, they were: cosmetic 75.39% ( $n = 1538$ ), lipodystrophy 8.33% ( $n = 170$ ), post-operative defects 4.71% ( $n = 96$ ), hemifacial atrophy 4.61% ( $n = 94$ ), other congenital malformations 2.11% ( $n = 43$ ), trauma 1.61% ( $n = 33$ ), burns 1.47% ( $n = 30$ ), scarring 1.13% ( $n = 23$ ) and other 0.69% ( $n = 14$ ).

**Table 1**

Overview of included studies characteristics and level of evidence.

Study	Year	Study design	Number of patients	Evidence level
Azzam et al. <sup>14</sup>	2013	Cohort	20	3
Baptista et al. <sup>15</sup>	2013	Case series	20	4
Castor et al. <sup>16</sup>	1999	Cohort	6	4
Caye et al. <sup>17</sup>	2003	Case series	29	4
Cervelli et al. <sup>18</sup>	2014	Case series	45	4
Chang et al. <sup>19</sup>	2013	Cohort	20	3
Coleman <sup>6</sup>	2006	Case series	3	4
Dollfus et al. <sup>20</sup>	2009	Case series	6	4
Duskova and Kristen <sup>21</sup>	2004	Case series	5	4
Erol and Agaoglu <sup>22</sup>	2013	Case series	2439	4
Ersek et al. <sup>23</sup>	1998	Case series	4	4
Fontedevila et al. <sup>24</sup>	2014	Randomized controlled trial	49	2
Fontedevila et al. <sup>25</sup>	2008	Case series	26	4
Gentile et al. <sup>26</sup>	2014	Cohort	20	3
Gerth et al. <sup>27</sup>	2014	Cohort	26	3
Gualdi et al. <sup>28</sup>	2005	Cohort	24	3
Guibert et al. <sup>29</sup>	2013	Case series	11	4
Guijarro et al. <sup>30</sup>	2011	Case series	11	4
Guyuron and Majzoub <sup>31</sup>	2007	Case series	16	4
Jianhui et al. <sup>32</sup>	2014	Cohort	36	3
Kanchwala et al. <sup>33</sup>	2005	Cohort	976	3
Khater et al. <sup>34</sup>	2009	Cohort	51	3
Kim et al. <sup>35</sup>	2010	Case series	6	4
Kuran and Tumerdem <sup>36</sup>	2005	Case series	71	4
Laurent et al. <sup>37</sup>	2006	Case series	9	4
Li et al. <sup>38</sup>	2013	Case control	38	4
Lim et al. <sup>39</sup>	2012	Case series	27	4
Mojallal et al. <sup>40</sup>	2015	Case series	100	4
Monreal <sup>41</sup>	2011	Case series	33	4
Ozkaya et al. <sup>42</sup>	2013	Case series	21	4
Rauso et al. <sup>43</sup>	2011	Cohort	23	4
Rusciani et al. <sup>44</sup>	2012	Case series	215	4
Sasaki <sup>45</sup>	2011	Case series	23	4
Schendel <sup>46</sup>	2015	Cohort	10	3
Stereodimas et al. <sup>47</sup>	2011	Cohort	20	3
Tsai and Liao <sup>48</sup>	2010	Case series	209	4
Wang et al. <sup>49</sup>	2015	Case series	105	4
Xie et al. <sup>50</sup>	2007	Case series	31	4
Xie et al. <sup>53</sup>	2010	Case series	83	4
Yin et al. <sup>51</sup>	2013	Case series	12	4
Yoshimura et al. <sup>13</sup>	2008	Cohort	6	4
Zeltzer et al. <sup>52</sup>	2012	Case series	250	4
Zhu et al. <sup>54</sup>	2016	Case series	22	4

### Injection characteristics

A total of 1875 procedures with clearly documented anatomic recipient sites were identified. The fat injection sites were divided according to anatomic facial regions treated, corresponding to upper ( $n = 393$ ), middle ( $n = 1234$ ) and lower third ( $n = 248$ ). The mean volume injected across all anatomical regions was 16.9cc (range 1–133cc). The mean volume by facial region was upper 11.8cc, middle 16.2cc and lower third 7.8cc.

### Follow-up

The mean follow up time was 13.95 months and median time was 12 months. The reported follow up periods ranged from 3 months to 50 months.

**Table 2**  
Study characteristics.

Characteristics	Overall n =
Patients treated	4577
Gender (%)	
Female	2516 (55)
Male	553 (12.1)
Unspecified	1508 (32.9)
Age (years)	
Mean	36.2
Range	7.4–80
Indication (%)	
Cosmetic	1538 (75.39)
Lipodystrophy	170 (8.33)
Post-op defects	96 (4.71)
Hemifacial atrophy	94 (4.61)
Congenital	43 (2.11)
Trauma	33 (1.61)
Burns	30 (1.47)
Scarring	23 (1.13)
Other	14 (0.69)
Volume injection (cc)	
Mean	16.9
Range	1–133
Injection sites (volume injected in cc)	
Upper	393 (11.8)
Middle	1234 (16.2)
Lower	248 (7.8)
Follow-up (months)	
Mean	13.95
Median	12

**Table 3**  
Detailed breakdown of fat harvesting techniques.

Technique	Number of patients	Number of studies
Coleman	676	21
Washing	403	8
Non-centrifuged	41	4
Low-pressure	152	4
Coleman + antibiotics	2439	1
Washed + centrifuged	10	1
Closed-membrane filtration	19	1
Total	3740	40

### Graft enrichment

Graft enrichment was documented in 2.38% of patients ( $n=109$ ) and consisted of either adipose tissue supplemented with stromal vascular fraction (SVF) ( $n=79$ ) or platelet rich plasma (PRP) ( $n=30$ ).

### Processing technique

A total of seven graft-processing techniques were documented in 38 studies. The Coleman technique was the most commonly used method across all studies. Two studies utilized more than one processing technique. Washing was performed using saline solution in all patients (Table 3).

**Table 4**  
Reported complications of fat grafting.

Complication	Number of patients	Percentage of all complications (%)
Asymmetry	74	71.15
Skin irregularities	14	13.46
Hypertrophy	4	3.85
Prolonged edema	4	3.85
Fat necrosis	3	2.88
Infection	2	1.92
Telangiectasias	1	0.96
Erythema	1	0.96
Activation of acne	1	0.96

**Table 5**  
Complications of fat grafting stratified according to site of injection.

Facial region	Complication	Number of complications (%)	Total number of injections
Upper Middle	Infection	1 (0.40)	248
	Asymmetry	9 (0.73)	1234
	Erythema	1 (0.08)	
	Hypertrophy	4 (0.32)	
	Skin irregularities	2 (0.16)	
Lower	Edema	1 (0.25)	393

**Table 6**  
Complications of fat grafting stratified according to procedural indication.

Indication	Complication	Number of complications (%)	Total number of injections
Cosmetic	Asymmetry	60 (3.90)	1538
	Fat necrosis	2 (0.13)	
	Infection	1 (0.06)	
Lipodystrophy	Asymmetry	11 (6.47)	170
	Hypertrophy	4 (2.35)	
Post-operative defect	Skin irregularities	3 (1.76)	
	Infection	1 (1.04)	96
	Telangiectasia	1 (1.04)	
Scar	Activation of acne	1 (4.35)	23
	Prolonged edema	1 (4.35)	
	Erythema	1 (4.35)	

### Harvest site

No preferred donor site was identified throughout the included studies. Adipose tissue was harvested from the abdomen, flanks, thighs, dorsal cervical hump, and buttocks, and was determined primarily based on surgeon and patient preference.

### Complications

An overall complication rate of 2.27% ( $n=104$ ) was noted amongst all studies. The most commonly documented complications were asymmetry, skin irregularities, hypertrophy, prolonged edema (lasting greater than 3 weeks), fat necrosis, infection, telangiectasia, erythema and activation of acne (Tables 4–6).

**Table 7**  
Detailed breakdown of the mean volume fat graft retention.

Characteristics (number of cases)	Retention percentage (%)
Indication	
Cosmetic (56)	45.76
Reconstructive (72)	38.26
Injection site	
Upper (61)	35.80
Middle (31)	41.50
Lower (12)	51.88
Processing technique	
Coleman (88)	41.00
Low-pressure (22)	44.53
Closed-membrane filtration (19)	41.20
Non-enriched (129)	41.63
Enriched	
SVF (56)	65.68
PRP (10)	69.00
Cosmetic SVF (36)	65.69
Reconstructive SVF (20)	65.65
Reconstructive PRP (10)	69.00
Coleman SVF (46)	65.17
Coleman PRP (10)	69.00
Washed + centrifuged SVF (10)	68.00

SVF, stromal vascular fraction; PRP, platelet-rich plasma.

### Volume retention at follow-up

The mean weighted volume of fat graft retention was stratified according to procedural indication, anatomical region of injection and processing technique. In addition, the mean retention was also calculated for grafts enriched with SVF and PRP.

Twelve studies documented the method used for quantifying the percentage of adipose tissue retained at follow-up. Two studies used two-dimensional photographs, six studies used a form of three-dimensional imaging, and four studies used computed tomography scanning (Table 7).

### Discussion

Autologous fat grafting has many beneficial qualities that make it advantageous for correcting contour deformities or augmenting soft-tissue for reconstructive or cosmetic indications. Fat grafts are autologous, biocompatible, permanent and viable when integrated into the injection site. They are easily accessible in most patients, and represent a relatively simple and low-cost surgical procedure. Many studies have demonstrated that in addition to the volume provided, adipose tissue contains both adipose-derived stem cells (ASC) as well as multipotent stem cells, which can differentiate into various tissue types.<sup>55–60</sup> Not only can ASCs differentiate into adipocytes and contribute to the regeneration of adipose tissue, but they have also been shown to promote angiogenesis through the release of growth factors in response to hypoxic microenvironments.<sup>55–60</sup> The fact that these growth factors influence the surrounding host tissue has been advantageously used to improve healing in conditions such as in radiation dermatitis or chronic ulcerations.<sup>60–63</sup>

The results of the present study serve to expand the existing body of literature and provide more complete evidence, pooled from the existing data, describing the effectiveness and safety of autologous fat grafting for the treatment of facial contour defects. This study illustrates the versatility of fat grafting, while also highlighting important details such as complication rates and rates of graft retention relative to anatomic regions of the face and processing techniques.

The complication rate (2.27%) identified in this review was minimal, with the majority of complications (84.61%) being attributed to either asymmetry or skin irregularities (excessive or inadequate grafting or graft survival). Fat necrosis ( $n = 3$ ) and infection ( $n = 2$ ) represented 2.88% and 1.92% of all

complications, respectively. These results differ from those seen in fat grafting used for both breast and gluteal augmentation. In the systematic review by Voglimacci et al.,<sup>7</sup> the authors reported a complication rate of 12.6% in cosmetic breast fat grafting. Of the 256 documented complications, there were 60 cases of fat necrosis (23.44% of all complications), and 18 cases of infection (7.03% of all complications). Conde-Green et al.<sup>64</sup> reported an overall complication rate of 7% in gluteal fat augmentation, of which there were 24 cases of infection (8.33% of all complications), and 23 cases of fat necrosis (7.99% of all complications).

Although not documented in this review, there have been anecdotal and published reports of significant patient morbidity and mortality as a result of fat emboli.<sup>10,65–68</sup> Cases of emboli following autologous fat grafting to the glabella and nose have been attributed to retrograde arterial injection, facilitated by the abundant vascular supply in these regions, notably the frontal and dorsal nasal arteries that are supplied by the ophthalmic artery.<sup>65–71</sup> Conversely, emboli in the gluteal region are often due to inadvertent injection into large caliber veins. Certain studies have therefore suggested using blunt cannulas to minimize this risk during injection in addition to aspiration prior to injection.<sup>10,72,73</sup> Unfortunately, there was insufficient data in the analyzed papers to validate this claim. In the present review, there were no reports of mortality or significant embolic complications associated with facial fat grafting procedures.

The mean volume of fat retained of non-enriched grafts was found to be 41.63% ( $n = 129$ ). The mean volume retained of fat enriched with SVF was 65.68% ( $n = 56$ ), while grafts enriched with PRP was 69% ( $n = 10$ ). Despite the limited sample size, discrepancy in the methods of fat volume retention assessment and follow-up intervals, these results parallel the survival of fat grafts to anatomical regions other than the facial region.<sup>7,8,10,74</sup> In a recent systematic review by Zhou et al.<sup>10</sup> evaluating graft survival based on technique, the authors reported a statistically significantly higher facial fat graft survival rate of 71% in the cell-assisted lipotransfer group as compared to 52% in the control group (standard fat grafting). It has been hypothesized that cell assisted-lipotransfer would increase fat survival by enhancing angiogenesis and adipogenesis.<sup>75,76</sup> However, current lipotransfer techniques are not reliably capable of reversing the central ischemia of larger volume grafts.<sup>63</sup>

The mean weighted volume of retained fat was stratified according to procedural indication, injection site and processing technique. The difference of retained volume in these subgroups was minimal. When comparing Coleman, low-pressure and closed-membrane filtration, the retained volumes were 41.00%, 44.53%, and 41.20%, respectively. These results are in keeping with a systematic review conducted by Gupta et al.,<sup>11</sup> in which the authors were unable to identify one processing technique that was superior to the others. It was postulated, however, that a combination of gentle washing and centrifugation should be employed to preserve adipocyte viability while removing the bulk of the contaminants. The studies included in this review that utilized washing as their graft processing technique did not publish graft survival rates.<sup>24,36,38,43,46,49,51,53</sup>

Graft retention for facial cosmetic and reconstructive indications was 45.76% and 38.26%, respectively. These results fall within the wide range of values reported for fat grafting to the breast (range 34%–82%).<sup>7–9,77</sup> Fat retention appears to be comparable for both cosmetic and reconstructive groups of patients, however, it was difficult to accurately assess given the vast spectrum of reconstructive indications, and the variability by which the retained volume was calculated. To that end, there is currently not enough data in the published literature to draw conclusions as to the superior indication (reconstruction vs. aesthetic) or processing technique for fat grafting.<sup>10,11,64</sup> Furthermore, a surrogate marker used to determine whether the outcome of the procedure was successful was patient and surgeon satisfaction. Objective measurement of satisfactory outcomes using questionnaires was only reported in a subset of studies, while the remainder relied on surgeon interpretation.<sup>14,18,22,29,30,34,35,40,49,50</sup>

Despite the comprehensive nature of this study, there are several inherent limitations of this review. The majority of the articles included were case series, with low levels of evidence, which introduces a risk of publication bias. The way in which information was documented and presented in the various included studies was heterogeneous. While some studies provided detailed demographics for each individual patient, others simply provided overall averages of their patient population, which prevented the use of a meta-analysis technique and statistical analysis to compare groups with the compiled data (i.e. complication rates by facial region or processing technique). Given that the

majority of complications were minor and likely more subjective depending on the surgeon, it is also possible that the true complication rates were underestimated. Heterogeneity in fat injection technique (i.e. syringe size, cannula size, rate of injection, volume of injection etc.) could significantly impact volume retention, a confounding factor that could not be accounted for in this review. Lastly, the methods used to assess graft survival varied in terms of length of follow-up (range 3–50.76 months) and method of volumetric analysis. Shorter follow-up may favor greater retained (reported) volume, as graft retention has been shown to stabilize between 5 and 12 months post-operatively.<sup>72,74</sup> Additionally, two of the twelve studies (16.7%) only utilized two-dimensional photography to assess graft retention, which allows for greater subjectivity when assessing the results.

The present study is the first systematic review of fat grafting in the facial region. Although limited in its ability to statistically analyze the published data, it does pool and summarize existing literature to provide a more comprehensive review of our current state of knowledge for this commonly performed procedure. Important information such as average retained grafting volumes and complication rates are presented to provide clinicians with more accurate information with which to guide their decision-making and patient education for facial fat grafting procedures.

## **Conflict of interest**

None.

## **Financial disclosure**

None of the authors has a financial interest in any of the products, devices, or drugs mentioned in this manuscript.

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## **Contribution of authors**

Dr. Jordan Gornitsky was involved in the review of the literature and data collection. He was also involved in manuscript write-up and the submission and revision of the manuscript.

Dr. Alex Viezel-Mathieu provided the original idea and was involved in the review of the literature and data collection. He was also involved in writing and editing the manuscript.

Dr. Nayif Alnaif supported the original idea and was involved in the write-up and revision of the manuscript.

Dr. Alain Joe Azzi was involved in the write-up and revision of the manuscript.

Dr. Mirko Gilardino is the supervisor/senior investigator of the project, provided technical/clinical guidance and supervised and was responsible for multiple revisions of the manuscript.

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