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What is the current optimal fat grafting processing technique? A systematic review

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ABSTRACT

Background: With the advents of new processing techniques and new graft survival theories in fat grafting, the question is: Which processing technique is of preference? This study systematically reviewed literature regarding current techniques for processing fat grafts.
Methods: PubMed, Embase, Cinahl, and Cochrane databases were searched until August 2015. Studies comparing different fat grafting processing techniques were included. Outcomes were viability of adipocytes, number of adipose-derived stromal/stem cells (ASC) and growth factors in vitro, volume and quality of the graft in animal studies, and satisfaction and volume retention in human studies.
Results: Thirty-five studies were included. Adipocyte viability and ASC numbers were the best using the gauze/towel technique (permeability principle) compared to centrifugation. With regard to centrifugation, the pellet contained more ASCs compared to the middle layer. The animal studies' and patients' satisfaction results were not distinctive. The only study assessing volume retention in humans showed that a wash filter device performed significantly better than centrifugation.
Conclusion: In this study, processing techniques using permeability principles proved superior to centrifugation (reinforced gravity principle) regarding viability and ASC number. Due to the variety in study characteristics and reported outcome variables, however, none of the processing techniques in this study demonstrated clinical evidence of superiority.

1. Introduction

Autologous fat transplantation (AFT) is a commonly applied procedure in reconstructive and aesthethic surgery (Coleman, 1997). Autologous subcutaneous fat is abundantly available in most patients, fully biocompatible, and conceivably permanent (Coleman, 2006). AFT is used for facial rejuvenation and correction of volume deficiencies caused by trauma (Arcuri et al., 2013), congenital malformations (Guibert et al., 2013), or after surgical procedures (Coleman, 2006). Moreover, AFT has been used increasingly for skin regeneration, e.g., in the case of burns and scars (Gentile et al., 2014).

Even though AFT has been performed for decades, no consensus exists about the best fat-grafting technique (Gir et al., 2012; Gupta et al., 2015). Among others, location of donor sites, use of local anesthetics, harvesting methods, processing techniques, and injection techniques continue to be points of discussion (Gir et al., 2012; Lin et al., 2015; Strong et al., 2015). Most studies have analyzed the effects of fat processing techniques on adipocyte viability (Gir et al., 2012). Currently used processing techniques are based on centrifugation, sedimentation, filtering, or washing principles (Gupta et al., 2015; Strong et al., 2015). Recent theories focus more on the crucial role of adipose-derived stromal/stem cells (ASC) (Matsumoto et al., 2006) and/or growth factors such as vascular endothelial growth factor (VEGF) (Nishimura et al., 2000; Garza et al., 2015) in fat graft survival rather than adipocyte viability. These theories give the current literature another perspective.

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This systematic review analyzed the effects of current processing techniques of fat grafting on adipocyte viability, levels of ASCs and growth factors in vitro, volume and quality of grafts in animal studies, as well as volume retention and patient satisfaction in human studies.

2. Material and methods

2.1. Information sources and search

PubMed, Embase, Cochrane Central Register of controlled trials, and Cinahl electronic databases were searched (last search August 10, 2015). Keywords used for the search were “fat graft”, “fat transfer”, “lipofilling”, “autologous fat transplantation”, or “subcutaneous fat transplant” in combination with either “processing”, “harvesting”, “centrifugation”, “gauze”, “mesh”, “towel”, “wash”, “sieve”, “sedimentation”, or “decantation” (Appendix 1). The reference lists of the selected articles were screened for relevant studies missed in the search.

2.2. Eligibility criteria

Papers were eligible if at least 2 different types of fat graft processes were compared or 1 process was compared to a control group without a processing procedure. In vitro, animal, and human studies were included when studies assessed adipocyte viability, ASC levels, stromal vascular fraction (SVF) yield, or growth factors in vitro, volume and quality of grafts in animals, or volume retention and patient satisfaction in humans. Studies focusing on methods other than processing of the harvested lipoaspirate were excluded. Moreover, studies were rejected when different harvesting techniques were used between study groups within a study or when additional growth factors, SVF, or ASCs were added to the lipoaspirate. Case series ($n < 5$), case reports, and expert reviews were also excluded. No language restrictions were applied.

2.3. Assessment of quality of included studies

The methodological quality of the included studies was assessed using the criteria of the modified Methodological Index of Non-randomized Studies (MINORS) (Slim et al., 2003). Table 1 describes the specific assessment criteria of the studies, specified for the current study. The authors.–> (A.J.T., P.N.D.) predefined a MINORS score of ≤ 6 as being of insufficient quality; those studies were excluded from analysis.

2.4. Study selection

Study selection and quality assessment was done by 2 observers independently (A.J.T., P.N.D.). Disagreement was discussed during a consensus meeting. In the case of a persistent disagreement, an independent observer (A.V.) gave a binding verdict.

2.5. Data items

Processing techniques used in the included studies were categorized according to the following conditions: “centrifugation”, “decantation”, “gauze/towel”, “devices”, “metal sieve”, “wash”, “wash and centrifugation”, and “negative control” (Table 2).

2.6. Outcomes

Studies were classified based on their outcome in vitro, in animals, and/or in humans. In vitro studies analyzed adipocyte viability, number ASC or SVF yield, and growth factors. Animal studies focused on volume retention (or graft weight) and/or histologic findings in transplanted grafts such as cysts, inflammation, fibrosis, vascularization, and/or integrity. Human studies focused on volume retention using three-dimensional (3D) imaging and/or patient or observer satisfaction using questionnaires or photographs.

2.7. Statistical analysis

Intraobserver agreement for MINORS assessment was calculated by an absolute agreement score and Cohen's kappa.

2.8. Publication bias of included studies

Publication bias could affect the results of this review. It might be more beneficial for research groups with an interest in processing devices to publish only those studies with positive results of their devices. Devices were split into another subcategory in the data analysis.

2.9. Synthesis of centrifugal forces

Centrifugal forces can be displayed in revolutions per minute or g force. Thus, to compare centrifugal forces of different studies, the relative centrifugal force (RCF) was used. If centrifugal forces were given in revolutions per minute (rpm), the RCF was calculated by the first author with the following formula: RCF (in $xg) = 1.12 \times 10^{-5} \times r \times rpm^2$ (Ohlendieck, 2010). This calculation means that the articles had to include the radius (r) of the

Table 1
Individual MINORS criteria explained.*

1. Aim	Clearly stated aim. Comparison and endpoints need to be mentioned.
2. Inclusion	Clear inclusion and exclusion criteria of subjects.
3. Collection	Prospective collection of data. Protocol established before the beginning of the study.
4. Endpoints	Endpoints need to be in accordance with the question/aim of the study. Endpoints need to be clearly stated.
5. Unbiased assessment	Any form of blinding (double blind or single blind).
6. Follow up	Follow up-period is sufficiently long to allow the assessment of the endpoints. In vitro studies = directly; In vivo >28 days; In vivo “long term” endpoint >10 months.
7. Loss to follow up	All patients should be included in a follow-up. Follow-up loss may not exceed 5%.
8. Prospective calculation of the study size	A sample size calculation is performed before the start of the study.
9. Adequate control group	The control group should have a gold standard. In this assessment any form of centrifugation is 1 point.
10. Contemporary groups	Control and studied groups are managed for the same time period (no historical comparison).
11. Baseline equivalence	Study groups are similar. No confounding factors. Fat from same person, or age/gender matched fat donors/receivers.
12. Statistical analysis	Adequate reported statistical analysis.

* Items are scored 0 (not reported or reported inadequately) or 1 (reported and adequate). The ideal score for comparative studies is 12.