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Clinical evidence of bio-stimulators for cervicofacial liposculpture: a systematic review

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Abstract

Introduction: In the liposculpture scenario, and at the cellular and molecular level, tissue engineering has numerous advantages that meet the needs of the injured tissue or organ for the regeneration process or fillings and contours. Biological microenvironments enable cell recognition and signaling cascades for neovascularization and stabilization of fat grafting. **Objective:** A concise systematic review was carried out on the use of potential biostimulators (cells and molecules) and the biochemical and physiological mechanisms that can contribute to the successful process of cervicofacial liposculpture, to promote neovascularization and stabilization of fat grafting or fat reduction. **Methods:** The systematic review rules of the PRISMA Platform were followed. The research was carried out from February to April 2022 in Scopus, PubMed, Science Direct, Scielo, and Google Scholar databases. The quality of the studies was based on the GRADE instrument and the risk of bias was analyzed according to the Cochrane instrument. **Results and Conclusion:** A total of 96 articles were found. A total of 36 articles were fully evaluated and 34 were included and developed in the present systematic review study. Considering the Cochrane tool for risk of bias, the overall assessment resulted in 11 studies at high risk of bias and 37 studies that did not meet the GRADE. The present study showed that the use of potential bio stimulators such as stromal vascular fraction cells and mesenchymal stem cells from adipose tissue, exosomes, microRNA, and PRP, as well as the molecules secreted by these cells, can contribute to the successful process of cervicofacial liposculpture, to promote neovascularization and stabilization of fat grafting or fat reduction. Furthermore, studies have shown that the use of adipose tissue plus PRP led to the presence of more pronounced inflammatory infiltrates and greater vascular reactivity, increased vascular permeability, and certain reactivity of the nervous component, noting that the addition of 20% PRP activated with calcium to adipose tissue grafts can enhance the results of regenerative and aesthetic facial surgeries.

Keywords: Facial liposculpture. Vascular stromal fraction. Mesenchymal stem cells. Platelet-rich plasma. Exosomes. MicroRNA.

Introduction

In the scenario of liposculpture, and at the cellular and molecular level, tissue engineering offers numerous advantages that meet the needs of the injured tissue or organ for the regeneration process or filling and contouring [1]. For this, it is necessary to understand the chemical, physical, and biological processes of both the biological material and the target biological niche [2,3].

In this sense, biological microenvironments enable cell recognition and signaling cascades for neovascularization and fat grafting stabilization [4]. Another advantage is the minimally invasive surgical intervention, which allows the use of faster surgical techniques that cause less risk to the patient [5,6]. Still,

adult stem cells, such as mesenchymal stem cells from adipose tissue (AMSC), are an alternative for cell therapy and human tissue engineering, since it was found that they have a high degree of plasticity, with the ability to of self-renewal and differentiation into specialized progenitors [7].

In this regard, AMSC are primordial mesodermal cells present in all tissues and are capable of differentiating in vitro and in vivo into different cell types. Its therapeutic potential is mainly explained by the production of bioactive molecules, which provide a regenerative microenvironment in injured tissues [8]. Furthermore, AMSC secretes a cascade of cytokines and growth factors with paracrine, autocrine, and endocrine activities, such as Il-6, Il-7, Il-8, Il-11, Il12, Il-14, Il-15, macrophage colony-stimulating factor (M-CSF), Flt-3 ligand and Stem Cell Factor (SCF), leukemia inhibitory factor (LIF), granulocytic colony-stimulating factor (G-CSF) and granulocytic colony-stimulating factor - macrophages (GM-CSF). These factors, when combined, can produce a series of responses from the local immune system, stimulating angiogenesis and inducing the proliferation and differentiation of mesenchymal stem cells in the desired tissue [9].

In addition, AMSC induces the expression of junction proteins and increases microvascular integrity and the production of nitric oxide (NO) by macrophages [8]. The stromal vascular fraction (SVF) derived from AMSC is a heterogeneous mixture of cells, including fibroblasts, pericytes, endothelial cells, blood cells, and stem cells derived from adipose tissue.

Furthermore, the platelet-rich plasma (PRP) and fibrin-rich plasma (FRP) developed in France by Choukroun et al. (1993) [10], shows the majority of leukocytes, platelets, and growth factors. It is the second generation of platelet concentrate with a high potential for wound repair. In this context, with progressive polymerization, the incorporation of circulating cytokines increases in the fibrin network, implying a longer life for these cytokines, as they will be released and used only in the remodeling of the initial scar matrix, which is long-term. Cytokines are thus kept available in situ for a convenient period when cells begin matrix remodeling [11,12].

In terms of biostimulation, adipose tissue stands out as an ideal filler for cosmetic surgery and is cheap and easily obtained, with a natural appearance and texture, immunologically compatible and long-lasting, and with a low risk of infection. By most metrics, autologous adipose tissue grafts perfectly meet these criteria. Facial fat grafting is a commonly accepted surgical procedure, and recent studies are working on the process of optimizing this technique, with a greater supply of cells and molecules for aesthetic improvement [4].

Thus, the present study carried out a concise systematic review of the use of potential bio stimulators (cells and molecules) and the biochemical and physiological mechanisms that can contribute to the successful process of cervicofacial liposculpture, to promote neovascularization and stabilization of fat grafting or lipo reduction.

Methods

Study Design

The systematic review rules of the PRISMA Platform were followed. Available at: www.prisma-statement.org/. Accessed in: 05/20/2023.

Data Sources and Research Strategy

The search strategies for this systematic review were based on the keywords (MeSH Terms): *"Facial liposculpture. Stromal vascular fraction. Mesenchymal stem cells. Platelet-rich plasma. Exosomes. MicroRNA"*. The research was carried out from February to April 2022 in Scopus, PubMed, Science Direct, Scielo, and Google Scholar databases. In addition, a combination of keywords with the Booleans "OR", "AND" and the operator "NOT" were used to target scientific articles of interest.

Study quality and risk of bias

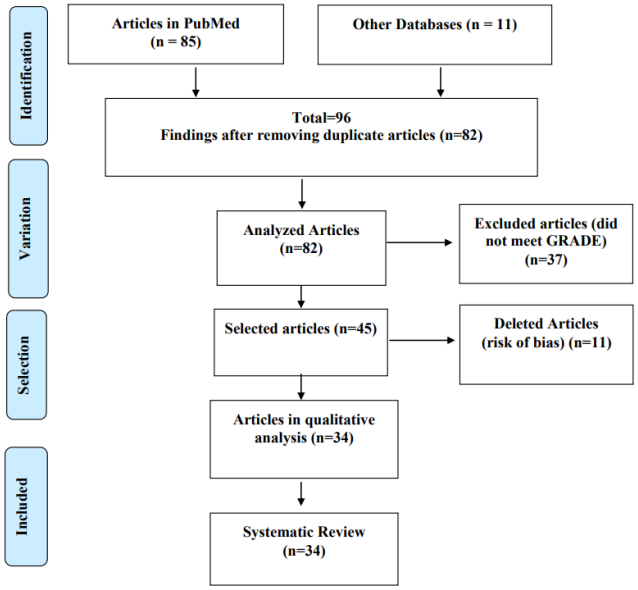
Study quality was based on the GRADE instrument [13] and the risk of bias was analyzed according to the Cochrane instrument [14].

Results and Discussion

Summary of Literary Findings

A total of 96 articles were found. Initially, duplication of articles was excluded. After this process, the abstracts were evaluated and a new exclusion was performed, removing the articles that did not include the theme of this article, resulting in 45 articles. A total of 36 articles were evaluated in full and 34 were included and developed in this systematic review study (**Figure 1**). Considering the Cochrane tool for risk of bias, the overall assessment resulted in 11 studies with a high risk of bias and 37 studies that did not meet GRADE.

Figure 1. Flowchart showing the article selection process.



Major Biostimulators for Liposculpture

Mesenchymal stem cells from adipose tissue (AMSC) are characterized by adhesion and proliferation properties, the ability to differentiate into osteocytes, chondrocytes, and adipocytes in vitro, positive for CD73, CD90 and CD105, and negative for the major histocompatibility complex class II (MHC-II), CD11b, CD14, CD31, CD34, and CD45. Due to their ability to differentiate, expand in vitro and release trophic materials, along with immunoregulatory properties, AMSC is a strong candidate for tissue repair [7-9].

Notably, due to the non-invasive isolation method, no ethical concerns, lower immunogenicity, faster self-renewal capacity, more stable doubling time, and higher proliferation potency, AMSC is the preferred candidate for cell and adipose tissue-based therapies in regenerative medicine [4]. In addition, Platelet-Rich Plasma (PRP) contains numerous growth factors responsible for its effectiveness. Growth factors are released after endogenous or exogenous platelet activation and then have a chemotactic effect and act directly and indirectly on tissue regeneration. Some platelets are activated by mechanical influences during centrifugation. Collagen activates platelets in vivo endogenously, while injection-induced needle bleeding may further contribute to clotting. Exogenous activation by adding calcium has become less popular in recent years [15].

The addition of PRP to adipose tissue grafts represented many advantages with a simple, economical, and safe method [4]. In addition to its potentiating effect on adipose tissue grafts, PRP has rejuvenating capabilities. Thus, adding 20% PRP to adipose tissue grafts is considered to offer better fat graft survival, less bruising and inflammation reaction, and easier application of adipose tissue grafts due to the liquefaction effect of PRP [16].

Added to this, exosomes stand out along with AMSC. Exosomes are extracellular vesicles with a size of 40-100 nm in diameter and a density of 1.13-1.19 g/mL, containing proteins, mRNAs, miRNAs, and DNAs. Exosomes change the biochemical characteristics of recipient cells through the delivery of biomolecules and play a role in cell communication. These vesicles are produced from body fluids and different types of cells. Evidence suggests that the AMSC-derived exosome (AMSC-EXO) exhibits AMSC-like functions with low immunogenicity and no tumorization [17].

In this sense, the composition of exosomes differs based on their sources. The protein and lipid content of exosomes was measured by various methods, such as fluorescence-activated cell sorting, Western blotting, mass spectrometry, and immunoelectron microscopy. In this regard, Rabs and Annexin, including Annexin I, II, V, and VI are cytosolic proteins present in exosomes that contribute to the formation of exosome docking, membrane fusion, and kinetic regulation of cytoskeletal membranes. Furthermore, adhesion molecules such as intercellular adhesion molecule-1, CD11a, CD11b, CD11c, CD18, CD9 adipose tissue globule, EGF-factor VIII (MFGE8), CD58, CD146, CD166 have also been identified in exosomes [18]. Exosomes also contain heat shock proteins (Hsp70 and Hsp90), which facilitate the loading of peptides into MHC I and II [19,20].

Also, exosomes contain non-coding RNAs or fragments, including overlapping RNA transcripts, protein-coding region, structural RNAs, fragments of transfer RNAs, YRNAs, short hairpin RNAs, small interfering RNAs (siRNAs), microRNA (miRNA), messenger RNA (mRNA) and DNA [21]. Regarding miRNA, exosomes present miR-1, miR-15, miR-16, miR-17, miR-18, miR-181 and miR-375 [22]. In addition, various cytokines such as Tumor Necrosis Factor-α (TNF-α), Granulocyte Macrophage Colony Stimulating Factor (GMCSF), Interleukin (IL)-2, IL-6, IL-8, IL-10, IL-15, IL-1β, are expressed in exosomes [23].

Major Clinical Findings

Adipose tissue grafts enriched with a stromal vascular fraction (SVF) were first reported by Moseley and colleagues in 2006 [24]. Later, it was better described by Matsumoto and colleagues [25], and soon after the technique was called "cell-assisted lipotransfer" (CLP). Since then, numerous preclinical studies in animals have demonstrated improvements in the volume of adipose tissue graft with CLP [26], giving rise to translational studies in humans.

In this regard, authors evaluated SVF-enriched adipose tissue grafts in 10 patients with Parry-Romberg

hemifacial atrophy and found that volume retention improved substantially in the group receiving CLP (47% resorption in control subjects versus 21% in CAL) [27]. In a tripleblind randomized clinical trial of 10 patients, authors found better retention in the group that received SVF-enriched adipose tissue grafts compared with standard adipose tissue grafts in the control group [28]. In addition, five human cohort studies have also been published examining SVF-enriched adipose tissue grafts in the face and chest. Four out of five studies showed improvement with CLP [29-32].

Also, a clinical study was performed on 13 patients who were candidates for a facelift. Patients underwent adipose tissue collection by liposuction from the abdomen and underwent one of three protocols: injection of adipose tissue enriched with SVF or stem cells derived from expanded adipose tissue, or adipose tissue plus PRP in the preauricular areas. As a result, the use of adipose tissue plus PRP led to the presence of more pronounced inflammatory infiltrates and greater vascular reactivity, increased vascular permeability, and certain reactivity of the nervous component. The addition of PRP did not improve the regenerative effect. Therefore, the use of PRP did not show significant advantages in skin rejuvenation over the use of stem cells derived from expanded adipose tissue or adipose tissue enriched with SVF [33].

To corroborate these findings with further scientific evidence, a meta-analysis study investigated the effect of PRP on the survival rate of fat grafting. Eleven studies with 1125 patients were analyzed. Patients were followed up from 3 to 24 months post-lip graft (PLG). The adipose tissue survival rate ranged from 20.5% to 54.8% in the PLG alone and from 24.1% to 89.2% in the PRP + PLG groups. The survival rate was significantly higher and the recovery time was significantly shorter in the PRP + PLG group than in the PLG alone group [34].

Thus, the scope of adding PRP to autologous PLG is to increase the graft survival rate. Upon activation, platelets release some important growth factors. As a result, PRP can enhance the proliferation and differentiation of AMSC into adipocytes, improve the vascularity of the adipose tissue graft, and can block the apoptosis of engrafted adipocytes. The other expected benefit of adding PRP to the adipose tissue graft is the improvement of skin trophic above the grafted areas. After the full analysis of 11 clinical studies in humans and 7 in animals, a significant increase in the survival rate of adipose tissue grafts was observed, highlighting that the addition of 20% PRP activated with calcium hydrochloride to adipose tissue grafts may enhance the results of regenerative and aesthetic facial surgeries [35].

Finally, a study investigated the safety and efficacy of PRP in 10 patients who received equal volumes of adipose tissue on opposite faces with plication of the lateral submuscular aponeurotic system or without a facelift. Comparable assessments of adipose tissue retention/baseline values by 3D Vectra Analysis were performed. The mean percent change in mean volume assessments at the adipose tissue/PRP sites from baseline demonstrated a higher, but not statistically significant value over 1 year than the percent value changes at the PRP/fat tissue sites. adipose/normal saline on the opposite face. Volume restorations of the malar fat pad, nasojugal sulcus, and nasolabial sulcus were evaluated. No adverse events were observed during the one-year study. Perioperative edema, erythema, bruising, and tenderness lasted up to 1 to 2 weeks at most [36].

Conclusion

The present study concluded that the use of potential bio stimulators such as cells from the vascular stromal fraction and mesenchymal stem cells from adipose tissue, exosomes, microRNA, and platelet-rich plasma, as well as the molecules secreted by these cells, can contribute to the successful process of cervicofacial liposculpture, to promote neovascularization and stabilization of fat grafting or fat reduction. Furthermore, studies have shown that the use of adipose tissue plus platelet-rich plasma led to the presence of more pronounced inflammatory infiltrates and greater vascular reactivity, increased vascular permeability, and certain reactivity of the nervous component, noting that the addition of 20% platelet-rich plasma activated with platelet-rich plasma calcium to adipose tissue grafts can enhance the results of regenerative and aesthetic facial surgeries.

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Ethical Approval

Not applicable.

Informed consent

Not applicable.

Data sharing statement

No additional data are available.

Conflict of interest

The authors declare no conflict of interest.

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References

1. Charles-de-Sá L, Gontijo-de-Amorim NF, Coleman S, Rigotti G. Regen Fat Code: A Standardized Protocol for Facial Volumetry and Rejuvenation. Aesthet Surg J. 2021 Oct 15;41(11):NP1394-NP1404. doi: 10.1093/asj/sjab016. PMID: 33453100.
2. Egro FM, Coleman SR. Facial Fat Grafting: The Past, Present, and Future. Clin Plast Surg. 2020 Jan;47(1):1-6. doi: 10.1016/j.cps.2019.08.004. Epub 2019 Oct 21. PMID: 31739886.
3. Farkas JP, Pessa JE, Hubbard B, Rohrich RJ. The science and theory behind facial aging. Plast Reconstr Surg Global Open. Apr 2013;1(1).
4. James IB, Coleman SR, Rubin JP. Fat, Stem Cells, and Platelet-Rich Plasma. Clin Plast Surg. 2016 Jul;43(3):473-88. doi: 10.1016/j.cps.2016.03.017. PMID: 27363761.
5. Lauritano D, Palmieri A, Candotto V, Carinci F. Regenerative Dentistry and Stem Cells: A Multilineage Differentiation as a Safe and Useful Alternative Way of Harvesting and Selection Adipose Derived Mesenchymal Stem Cells. Curr Drug Targets. 2018;19(16):1991-1997. doi: 10.2174/1389450119666180816122230. PMID: 30112989.
6. Avantaggiato P, Avantaggiato P, Piva A, Candotto V, Moreo G. Mesenchimal stem cells in oral medicine: an overview. J Biol Regul Homeost Agents. 2020 May-Jun;34(3 Suppl. 1):99-105. DENTAL SUPPLEMENT. PMID: 32618167.
7. Dominici M, Le Blanc K, Mueller I, Slaper-Cortenbach I, Marini FC, Krause DS, Deans RJ, Keating A, Procko DJ, Horwitz EM. Minimal criteria for defining multipotent mesenchymal stromal cells. The International Society for Cellular Therapy position statement. Cytotherapy, 2006, v. 8, n. 4, p. 315-317.
8. Zuk PA, Zhu M, Ashjian P. Human adipose tissue is a source of multipotent stem cells. Mol Biol Cell; 13: 4279–4295, 2002.
9. Caplan AI, Buder SP. Mesenchymal stem cells: building blocks for molecular medicine in the 21st century. Trends Mol Med; 7: 259-64, 2001.
10. Choukroun J, Diss A, Simonpieri A, Girard M, Schoeffler C, Dohan SL. Platelet-rich fibrin (PRF): a second-gereration platelet concentrate. Part V: histologic evaluations of PRF effects on bone allograft maturation in sinus lift. O Surg Oral Med Pathol Radiol Endod 2006; 101(3):299-303.
11. Del Corso, M, Toffler M, Ehrenfest D. Use of Autologous Leukocyte and Platelet-Rich Fibrin (L-PRF) Membrane in Post-Avulsion Sites: An Overview of Cjoukroun's PRF. The Journal of Implant and Advanced Clinical Dentistry, 2010; 1:27-35.
12. Ehrenfest D, Rasmusson L, Albrektsson T. Classification of platelet concentrates: from pure platelet-rich plasma (P-PRP) to leucocyte- and platelet-rich fibrin (L-PRF). Cell Press, 2009; 27.
13. H Balshem H, Grade guidelines: 3 ratng the quality of evidence. Journal of Clinical Epidemiology, Maryland Heights, 64 (4) (2011) 401-406.
14. Higgins, S Green, Cochrane Handbook for Systematic Reviews of Interventions. Version 5.1.0 [updated March 2011]. The Cochrane Collaboration; 2011.
15. Emer J. Platelet-Rich Plasma (PRP): Current Applications in Dermatology. Skin Therapy Lett. 2019 Sep;24(5):1-6. PMID: 31584784.
16. Modarressi A. Platlet Rich Plasma (PRP) Improves Fat Grafting Outcomes. World J Plast Surg. 2013 Jan;2(1):6-13. PMID: 25489498; PMCID: PMC4238337.
17. C. Thery, M. Boussac, P. Veron, P. Ricciardi-Castagnoli, G. Raposo, J. Garin, et al., Proteomic analysis of dendritic cell-derived exosomes: a secreted subcellular compartment distinct from apoptotic vesicles, J. Immunol. 166 (2001) 7309–7318.
18. Baharlooi H, Nouraei Z, Azimi M, Moghadasi AN, Tavassolifar MJ, Moradi B, Sahraian MA, Izad M. Umbilical cord mesenchymal stem cells as well as their released exosomes suppress proliferation of activated PBMCs in multiple sclerosis. Scand J Immunol. 2020 Dec 18:e13013. doi: 10.1111/sji.13013. Epub ahead of print. PMID: 33338274.
19. R. Mears, R.A. Craven, S. Hanrahan, N. Totty, C. Upton, S.L. Young, et al., Proteomic analysis of melanoma-derived exosomes by two-dimensional polyacrylamide gel electrophoresis and mass spectrometry, Proteomics 4 (2004) 4019–4031, https://doi.org/10.1002/pmic.200400876.
20. R. Gastpar, M. Gehrmann, M.A. Bausero, A. Asea, C. Gross, J.A. Schroeder, et al., Heat shock protein 70 surface-positive tumor exosomes stimulate

migratory and cytolytic activity of natural killer cells, Cancer Res. 65 (2005) 5238–5247, https://doi.org/10.1158/0008-5472.can-04-3804.
21. W. Xu, Z. Yang, N. Lu, From pathogenesis to clinical application: insights into exosomes as transfer vectors in cancer, J. Exp. Clin. Cancer Res. 35 (2016) 156, https://doi.org/10.1186/s13046-016-0429-5.
22. H. Valadi, K. Ekstrom, A. Bossios, M. Sjostrand, J.J. Lee, J.O. Lotvall, Exosomemediated transfer of mRNAs and microRNAs is a novel mechanism of genetic exchange between cells, Nat. Cell Biol. 9 (2007) 654–659, https://doi.org/10.1038/ncb1596.
23. B. Zhang, L. Shen, H. Shi, Z. Pan, L. Wu, Y. Yan, et al., Exosomes from Human Umbilical Cord Mesenchymal Stem Cells: Identification, Purification, and Biological Characteristics, 2016 (2016), p. 1929536, https://doi.org/10.1155/2016/1929536.
24. Moseley TA, Zhu M, Hedrick MH. Adipose-derived stem and progenitor cells as fillers in plastic and reconstructive surgery. Plast Reconstr Surg 2006; 118:121S–8S.
25. Matsumoto D, Sato K, Gonda K, et al. Cell-assisted lipotransfer: supportive use of human adiposederived cells for soft tissue augmentation with lipoinjection. Tissue Eng 2006;12:3375–82.
26. Toyserkani NM, Quaade ML, Sørensen JA. Cell-assisted lipotransfer: a systematic review of its efficacy. Aesthetic Plast Surg 2016. http://dx.doi.org/10.1007/s00266-016-0613-1.
27. 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 3dimensional camera. Ann Plast Surg 2012;69:331–7.
28. Kolle S-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):1113–20.
29. Gentile P, Orlandi A, Scioli MG, et al. A comparative translational study: the combined use of enhanced stromal vascular fraction and platelet-rich plasma improves fat grafting maintenance in breast reconstruction. Stem Cells Transl Med 2012;1(4):341–51.
30. Li J, Gao J, Cha P, et al. Supplementing fat grafts with adipose stromal cells for cosmetic facial contouring. Dermatol Surg 2013;39(3 Pt 1):449–56.
31. Chang Q, Li J, Dong Z, et al. Quantitative volumetric analysis of progressive hemifacial atrophy corrected using stromal vascular fractionsupplemented autologous fat grafts. Dermatol Surg 2013;39(10):1465–73.
32. Gentile P, De Angelis B, Pasin M, et al. Adiposederived 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):267–72.
33. Rigotti G, Charles-de-Sá L, Gontijo-de-Amorim NF, Takiya CM, Amable PR, Borojevic R, Benati D, Bernardi P, Sbarbati A. 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 Mar;36(3):261-70. doi: 10.1093/asj/sjv231. PMID: 26879294; PMCID: PMC5127465.
34. Wu M, Karvar M, Liu Q, Orgill DP, Panayi AC. Comparison of Conventional and PlateletRich Plasma-Assisted Fat Grafting: A Systematic Review and Meta-analysis. J Plast Reconstr Aesthet Surg. 2021 Nov;74(11):2821-2830. doi: 10.1016/j.bjps.2021.05.046. Epub 2021 Jun 12. PMID: 34246590.
35. Picard F, Hersant B, La Padula S, Meningaud JP. Platelet-rich plasma-enriched autologous fat graft in regenerative and aesthetic facial surgery: Technical note. J Stomatol Oral Maxillofac Surg. 2017 Sep;118(4):228-231. doi: 10.1016/j.jormas.2017.05.005. Epub 2017 May 30. PMID: 28576462.
36. 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 May 16;39(6):675-686. doi: 10.1093/asj/sjy254. PMID: 30534955.

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