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Review

Regenerative Stem Cell Therapy in Fat Grafting: Article Review

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ABSTRACT

Regenerative therapy with stem cells in fat grafting has emerged as a promising strategy to improve graft survival and tissue quality. The application of adipose-derived stem cells (ADSCs) enhances angiogenesis, reduces fat resorption and promotes tissue remodeling, overcoming limitations of conventional lipotransfer techniques. Preclinical studies show that ADSCs secrete angiogenic factors such as VEGF and HGF, improving local neovascularization and graft integration. Initial clinical trials demonstrate greater volume retention and reduced fibrosis in cell-assisted grafts compared to pure fat grafts. However, variation in protocols for ADSC isolation, cultivation and concentration hinders result standardization and direct comparison between studies. Another concern involves safety: although most studies report no significant adverse events, long-term follow-up is needed to evaluate theoretical risks, such as potential tumorigenesis. This review analyzes the mechanisms of action of ADSCs in fat grafting, outlines key cell preparation methods and describes relevant clinical outcomes. Regulatory challenges, ethical issues and future perspectives are also discussed, including bioengineering techniques and three-dimensional scaffolds to optimize regenerative therapy. Finally, the urgency of randomized, multicenter and long-term studies is emphasized to consolidate evidence of efficacy and safety, aiming at the clinical incorporation of this approach in soft tissue reconstruction and harmonization.

Keywords: Fat grafting; Adipose-derived stem cells; Cell-assisted lipotransfer; Angiogenesis; Tissue regeneration

Introduction

Autologous fat grafting is widely employed in reconstructive and aesthetic plastic surgery to correct volume defects and body contour irregularities. However, the resorption rate varies from 20% to 70%, often requiring repeated procedures to maintain satisfactory outcomes. To overcome these limitations, researchers have incorporated adipose-derived mesenchymal stem cells (ADSCs) into fat grafts, creating what is termed "cell-assisted lipotransfer" (CAL). ADSCs display high proliferation capacity and secrete paracrine angiogenic and anti-apoptotic factors, contributing to improved graft viability and recipient site integration. The pioneering method proposed by Yoshimura, et al. involves isolating nano fat[1], centrifuging lipoaspirate samples and retrieving the "stem cell pellet," which is then reinjected with adipose tissue during the same surgical procedure. This technique demonstrated significantly increased volume retention in initial clinical studies on breast augmentation and facial filling. Rigorous preclinical animal studies validated that ADSCs promote capillary formation via VEGF, FGF-2 and HGF release and modulate local inflammatory responses. Despite improvements in graft survival, preparation protocols vary widely. Some groups use enzymatic digestion with collagenase to obtain the stromal vascular fraction (SVF), while others prefer less invasive mechanical methods to reduce cost and complexity.

Variability in the number of injected cells per volume of fat hampers data comparison and the creation of standardized clinical guidelines. Regulatory issues also limit CAL's clinical diffusion. In regions like the United States and European Union, procedures involving substantial cell manipulation are subject to stringent regulatory scrutiny, delaying routine adoption. Ethically, patients must be fully informed of the risks and benefits of experimental cell therapies, including the need for long-term follow-up to monitor potential adverse outcomes, such as neoplasm formation.

Objectives

This review aims to synthesize the current knowledge on regenerative therapy with ADSCs in fat grafting, detailing mechanisms of action, cell preparation methodologies, preclinical and clinical evidence, as well as future challenges and perspectives.

Materials and Methods

A literature review was conducted using the databases PubMed, SciELO, Google Scholar and ScienceDirect.

Discussion

Results from animal models of ADSC-enriched lipotransfer highlight the significant impact of these progenitors on tissue engraftment. In rats, Zhou, et al. observed 1.5 times greater volume retention in ADSC-assisted grafts compared to pure grafts[2], attributed to microvascular formation and reduced cell apoptosis. Similarly, Rigotti, et al. demonstrated improved healing in irradiated tissues, with enriched lipoaspirate transplants reducing fibrosis and improving dermal elasticity[3]. Molecular mechanisms involve both direct transdifferentiation of ADSCs into endothelial cells and paracrine effects via growth factor release that recruits resident progenitor cells and modulates inflammation. In clinical settings, Yoshimura, et al. reported higher patient satisfaction in CAL-assisted breast augmentation[1], with over 80% volume retention after six months compared to 50% in controls. Parikh & Kim, in a systematic review[4], found that adding ADSCs reduced the amount of fat required by an average of 30% to achieve comparable outcomes, while also decreasing fat necrosis-related complications. However, study heterogeneity limits definitive conclusions. Ferraro, et al. noted that differences in cell viability post-cryopreservation significantly impact graft effectiveness and no consensus exists on optimal storage techniques[5]. Furthermore, Benjamin, et al. compared PRP and ADSCs for enrichment[6], finding similar results, suggesting multiple paracrine elements may serve as lipotransfer adjuvants.

Regarding safety, Györgyi, et al. reviewed MCAS reports on cell therapy adverse events and found no increase in neoplasms or serious complications over five years of follow-up[7], though they recommend larger long-term studies. The absence of adverse event reports does not eliminate the need for surveillance, particularly in oncologic or immunocompromised patients. Advances in bioengineering, such as 3D scaffolds and ADSC bioreactors, may improve cell production standardization and graft viability. Planat-Bénard, et al. demonstrated the differentiation of ADSCs into endothelial cells within biomimetic scaffolds[8], paving the way for prevascularized grafts. Kato, et al. introduced bioreactors capable of producing functional adipose tissue in vitro[9], potentially reducing clinical variability and enhancing safety[10-15].

Conclusion

Regenerative therapy with ADSCs in fat grafting represents a significant advancement in reconstructive and aesthetic surgery, offering greater volume retention, improved vascularization and controlled tissue remodeling. Multiple mechanisms contribute to these benefits, including paracrine effects and direct cell differentiation, facilitating angiogenesis, apoptosis inhibition and fibrosis modulation. Although current clinical studies support enhanced graft survival and patient satisfaction, methodological heterogeneity - from cell isolation to enrichment protocols - impedes direct comparisons and the creation of standardized guidelines. Regulatory and ethical challenges also hinder the routine application of this technique, necessitating controlled, randomized, multicenter trials to evaluate efficacy, safety and cost-effectiveness in the medium to long term. Future perspectives include developing prevascularized scaffolds, standardized ADSC expansion bioreactors and combined approaches using purified growth factors or controlled-release systems. Efficient cryopreservation strategies may also enable "off-the-shelf" therapies, expanding patient access to cell-assisted lipotransfer. In conclusion, while results are promising, the full clinical adoption of stem cell regenerative therapy depends on robust evidence and regulatory progress. The maturation of this technology may transform the field of soft tissue surgery, offering safer, more effective and longer-lasting treatments worldwide.

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