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ADVANCES IN THE USE OF PLATELET-RICH PLASMA AND ADIPOSE TISSUE DERIVATIVES IN SURGICAL REGENERATIVE MEDICINE

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Background. Adipose-derived tissues and platelet-rich plasma (PRP) have emerged as promising agents in regenerative medicine and aesthetic surgery due to their ability to stimulate tissue repair, enhance angiogenesis, and reduce inflammation. Their combined use has gained increasing attention in reconstructive and plastic surgical practices.

Aim. This review aims to evaluate the biological functions and clinical potential of adipose tissue derivatives and PRP in surgical applications, particularly in enhancing fat graft survival and promoting tissue regeneration.

A systematic review of scientific literature was performed using databases such as *PubMed*, *Scopus*, and *Web of Science*, following PRISMA guidelines. The selection criteria included original studies, reviews, and clinical trials focused on the biological properties, therapeutic mechanisms, and surgical outcomes associated with the use of adipose tissue and PRP. Adipose tissue contains multipotent mesenchymal stem cells that contribute to neovascularization, immune modulation, and extracellular matrix remodeling. PRP is rich in growth factors that support cellular proliferation, tissue integration, and inflammation control. The co-administration of PRP with fat grafts improves graft retention and healing outcomes. Several clinical studies demonstrate enhanced aesthetic and functional results in procedures involving facial reconstruction, wound healing, and breast surgery.

Conclusion. The integration of PRP and adipose-derived therapies offers significant advantages in surgical regenerative strategies. However, heterogeneity in preparation methods and application protocols limits comparability across studies. Further research is necessary to standardize techniques, validate outcomes, and broaden the clinical applicability of these regenerative modalities.

Key words: platelet-rich plasma; adipose tissue; regenerative medicine; fat grafting; surgery

INTRODUCTION

Adipose tissue is recognized as a complex and dynamic organ that not only participates in energy metabolism but also possesses considerable regenerative capabilities, primarily due to the presence of mesenchymal stem cells. Over the past decade, it has become increasingly utilized in the field of regenerative medicine, with particularly widespread application in plastic and reconstructive surgery, where lipofilling techniques continue to evolve and improve [12].

Simultaneously, platelet-rich plasma (PRP) has emerged as a complementary therapeutic modality, offering pro-angiogenic and immunomodulatory benefits that may enhance the effectiveness of fat grafting procedures.

This review focuses on evaluating the biological properties of adipose tissue and current lipofilling approaches, as well as exploring the synergistic effects of PRP when used in combination with fat grafts. Particular attention is given to their potential integration into various clinical contexts, including tissue repair, aesthetic procedures, and surgical reconstruction.

To conduct a thorough and structured literature review, we applied a detailed search strategy using several major electronic databases: PubMed, Scopus, Web of Science, Embase, and the Cochrane Library. The search encompassed publications from January 2022 to December 2023 and targeted high-quality sources in regenerative medicine, plastic and reconstructive surgery, and adipose-derived therapies. We formulated search queries using a combination of keywords and controlled vocabulary (MeSH terms), including «adipose tissue», «adipose-derived stem cells»(ASCs), «stromal vascular fraction» (SVF), «platelet-rich plasma» (PRP), «lipofilling», «fat grafting», «graft survival», and other related concepts. Boolean operators (AND, OR) were employed to refine and broaden the results where appropriate.

Inclusion criteria were restricted to peer-reviewed English-language publications released between 2000 and 2023, prioritizing original studies, randomized controlled trials, systematic reviews, and meta-analyses that addressed the biological mechanisms, therapeutic applications, and clinical integration of adipose tissue and PRP.

Excluded from consideration were case reports, commentaries, abstracts without full-text access, articles with limited methodological transparency, and works unrelated to the main research focus.

From an initial pool of 1,250 records, duplicate entries were removed, yielding 850 unique titles and abstracts for preliminary evaluation. Following this screening, 300 articles were selected for full-text review. Ultimately, 150 studies were deemed suitable for inclusion based on methodological quality and alignment with our review objectives. Key information—such as study type, patient population, technical parameters of PRP and fat processing, and relevant clinical outcomes (e.g., graft retention, vascularization, and efficacy)—was systematically extracted using standardized data collection forms.

ADIPOSE TISSUE AND ITS IMPORTANCE IN MEDICINE

Structural and Functional Features of Adipose Tissue. Adipose tissue is a metabolically active and heterogeneous organ composed of mature adipocytes and various stromal-vascular elements, including preadipocytes, fibroblasts, immune and endothelial cells, as well as adipose-derived stem cells. It consists of two primary components: adipocytes, responsible for lipid storage, and the stromal vascular fraction (SVF), which provides regenerative potential through its content of multipotent stem and support cells [17].

Adipogenesis follows a two-phase process – initial commitment of mesenchymal cells into preadipocytes, followed by terminal differentiation marked by lipid accumulation. This capacity declines with aging [47]. Traditionally, adipose cells were categorized as white (WAT) or brown (BAT), but recent findings have revealed intermediate subtypes such as beige adipocytes, which exhibit thermogenic properties under stimuli like cold exposure or exercise. Pink adipocytes, described in rodent models during lactation, show epithelial-like traits, though their presence in humans remains uncertain [71].

White adipocytes store energy in a single lipid droplet and produce regulatory hormones like leptin and adiponectin [100], while brown adipocytes possess multilocular lipid droplets and abundant mitochondria, supporting heat production [21]. Adipocytes are structurally fragile, whereas preadipocytes show greater resilience due to their size and metabolic profile [38]. The surrounding extracellular matrix, rich in collagen and adhesive proteins, maintains tissue architecture and vascular support [104]. Additionally, adipose tissue acts as an endocrine organ, secreting various adipokines and cytokines that influence systemic metabolism, inflammation, and tissue homeostasis [13].

The Role of Adipose Tissue in Regenerative Medicine. Adipose tissue is a key source in regenerative medicine, offering a higher yield of adult stem cells than bone marrow [32, 38]. These adipose-derived stem cells (ASCs) possess strong regenerative and immunomodulatory abilities, migrating to injury sites to support healing. The stromal vascular fraction (SVF), extracted from digested adipose tissue, contains diverse stromal and immune cells that act mainly via paracrine mechanisms, particularly in low-oxygen conditions [38]. Pre- and intraoperative use of platelet-rich plasma (PRP) has been shown to improve fat graft retention, vascularization, and reduce inflammation, leading to better tissue integration [32]. ASCs produce key growth factors like vascular endothelial growth factor (VEGF), HGF, and FGF2, aiding angiogenesis and tissue repair [38]. Additionally, adipocytes can dedifferentiate, and progenitor cells can become fibroblasts, keratinocytes, and endothelial cells.

Fat grafting has shown clinical benefits in treating burns, osteoarthritis, and chronic wounds [115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126], particularly by enhancing angiogenesis in poorly perfused diabetic tissues [24]. SVF makes up ~10% of non-parenchymal adipose content and includes endothelial, mesenchymal, and immune cells. These cells modulate inflammation and stimulate matrix remodeling; for example, IL-10-secreting macrophages aid tissue repair [143]. SVF injections improve wound healing and scar quality, enhancing texture, elasticity, and hydration [139]. Due to its accessibility, biocompatibility, and stem cell richness, adipose tissue is a valuable and versatile material in regenerative medicine and lipofilling procedures [61].

LIPOFILLING IN PLASTIC SURGERY

Historical Development and Contemporary Techniques. Lipofilling, defined as the autologous transplantation of adipose tissue acquired through liposuction, has experienced notable evolution over time. Historically, its progression can be categorized into three distinct eras: the initial phase from 1889 to 1977, characterized by fat excision techniques; a second period between 1977 and 1994, when liposuction procedures were still invasive and traumatic; and a third stage commencing in 1994, marked by the introduction and refinement of the Coleman method [107]. The earliest recorded instance of using fat for reconstructive purposes dates back to 1889, when Meulen V. utilized omental tissue in the repair of a hernia [106]. In 1893, Neuber G. performed the first documented fat grafting by transferring adipose tissue from the arm to the orbital region, highlighting the superior outcomes associated with small-volume grafts [109]. Czerny subsequently used a lipoma for breast reconstruction following mastectomy, laying the groundwork for fat-based augmentation techniques [5].

In 1910, Lexer applied fat grafting in facial aesthetic procedures and for the correction of deformities, including cases of Dupuytren's disease [19]. Brunning incorporated fat grafting into rhinoplasty surgeries in 1911, while Holländer explored cross-species fat transplantation, though his methods did not gain widespread acceptance [44]. By the mid-20th century, the method had further advanced when Billings and May advocated for its use in breast reconstruction and recommended the inclusion of fascia to enhance graft longevity [40]. Notably, during World War II, fat grafting was reportedly employed in espionage-related facial modifications [107]. Peer later demonstrated that only approximately half of the transplanted adipocytes survived, thereby emphasizing the necessity of refining surgical techniques [22].

The practice of liposuction, initially introduced in the 1970s by Arpad and Fischer, underwent significant improvement through the contributions of Illouz, who employed blunt-tipped cannulas, revolutionizing adipose harvesting methods [81]. In the 1980s, surgeons such as Ellenbogen and Bircoll began utilizing fat grafting for the correction of facial asymmetries and breast irregularities, although its broader application was limited by oncological safety concerns [118]. The 1990s introduced a series of innovations, including the development of fat-filled implants (Hang-Fu) and enhanced graft processing techniques (Chajchir) [74,51]. The Coleman method, which prioritized gentle aspiration, careful fat purification, and precise microinjection, significantly improved both graft viability and outcome consistency [56].

In the current clinical landscape, lipofilling is employed not only for volumetric restoration but also as a therapeutic intervention for scar remodeling, wound healing, and overall aesthetic enhancement. Its expanding scope of applications underscores its enduring relevance and utility in both reconstructive and aesthetic plastic surgery.

Principal Stages and Hypotheses Regarding Fat Graft Viability. Although substantial research has been dedicated to fat grafting, a universally accepted standard for adipose tissue harvesting and processing has yet to be established [45]. The procedural framework generally comprises three key stages: (1) harvesting fat via liposuction, (2) subsequent processing, and (3) reinjection of the prepared graft. The widely adopted Coleman technique, developed in the 1990s, involves low-pressure manual aspiration aimed at minimizing cellular trauma, followed by centrifugation to segregate the harvested fat into distinct layers: oil, a central adipocyte-rich fraction, and debris. The middle fraction, enriched with viable adipocytes and stromal vascular cells, is then reimplanted in small, controlled quantities to foster new blood vessel formation [55].

Numerous alterations to the original method have since emerged [123]. In some protocols, centrifugation is replaced by simpler techniques such as gravitational decanting or filtration through sterile gauze or Ringer's solution [92]. Commercially available systems now strive to maximize the recovery of viable cells while reducing procedural trauma [43]. A consensus review by Kaufman et al. indicated that neither the donor site nor the processing method significantly influenced clinical outcomes. Nonetheless, it is common surgical practice to overcompensate during grafting to account for an anticipated volume reduction of up to 50% within six months postoperatively [86].

The effectiveness of fat grafting is contingent upon the viability and type of transplanted cells – whether mature adipocytes, preadipocytes, or mesenchymal stem cells – as well as the thorough removal of contaminants such as residual blood, which may compromise integration and survival [85]. Certain theoretical models suggest that the majority of grafted adipocytes fail to persist, and instead, regeneration is mediated by the activation of host cells at the implantation site. The precise cellular composition that ensures long-term engraftment success, however, remains under investigation.

Another variable that may influence graft outcomes is the diameter of the cannula used during harvesting and injection, although empirical data on this factor are sparse. Discrepancies in clinical results can often be attributed to variations in technique, individual patient characteristics, and gaps in understanding the biological behavior of fat tissue, especially in relation to aging. The Coleman method typically employs adipose tissue harvested from the abdominal or hip regions, followed by centrifugation to isolate the desired graft material, which contains both mature fat cells and components of the stromal vascular fraction [56]. Due to the inherently low vascular density of fat, graft retention is often unpredictable. Adipocytes are highly sensitive to oxygen deprivation, making prompt revascularization a critical determinant of graft survival. If blood flow is restored quickly, the potential for recovery improves considerably [29]. Extended graft viability not only supports sustained secretion of trophic factors but also enhances the regenerative capacity by maintaining stem cell activity.

Platelet-Rich Plasma: Definition, Typology, and Production Methods

The post-transplant fate of fat grafts is strongly shaped by interactions with the extracellular matrix, which regulates essential cellular processes such as migration, differentiation, and proliferation. Several conceptual frameworks have been proposed to explain the survival dynamics of grafted fat. Peer's Graft Survival Theory posits that adipocytes initially survive through diffusion of plasma nutrients, with smaller graft volumes demonstrating enhanced outcomes due to superior nutrient diffusion [22]. The Graft Replacement Theory argues that most transplanted adipocytes undergo apoptosis, and regeneration is instead driven by stromal vascular fraction (SVF) cells, which induce angiogenesis and adipogenesis [120]. Conversely, the Host Cell Replacement Theory suggests that all necrotic donor cells are supplanted by host-derived adipocytes, connective tissue, and vasculature, thus placing emphasis on the recipient site's biological environment [110].

According to Eto et al. (2012), three distinct zones can be identified within a fat graft: an external viable zone measuring approximately 300 μm, a middle zone characterized by regenerative activity and partial cell death (600–1200 μm), and a central necrotic zone devoid of viable cells. Revascularization typically begins within 48 hours, but in the absence of sufficient perfusion, cells in the deeper layers rapidly undergo necrosis [63,117]. While adipogenesis can restore tissue volume over a period of three months, complete structural integration may take up to nine months and may still result in partial resorption or fibrotic transformation [19].

Long-term volume retention varies considerably, with reported losses reaching as high as 80% [129]. Graft success is influenced by multiple variables, including the technique used, individual patient factors such as age and body mass index, comorbid conditions, and the efficiency of neovascularization. Mechanical trauma during injection and insufficient angiogenesis are notable contributors to reduced graft longevity [140, 27]. Empirical studies underscore the importance of early revascularization, revealing a direct correlation between prompt blood vessel formation and improved graft retention rates [46]. Recipient site optimization is crucial for fat graft success. Strategies include cyclic negative pressure to enhance perfusion [80], and the use of alloplastic implants to slow resorption via controlled inflammation [97]. VEGF application improves vascular growth and reduces oil cysts [137]. Ischemic preconditioning and microneedling stimulate oxygenation and matrix remodeling [8,127]. Preclinical evidence suggests that pre-treatment with PRP can enhance graft integration, though comparative data with other techniques remain limited. Further research is necessary to standardize recipient site preparation and improve clinical outcomes [82].

COMBINED USE OF PRP AND LIPOFILLING

Platelet-rich plasma (PRP) is defined as plasma with platelet concentrations significantly higher than baseline [6, 42, 53, 103, 111]. Due to varied preparation protocols, its composition – particularly platelet, leukocyte, and growth factor content – differs widely across over 17 commercial systems [34, 75]. While Marx and Cho proposed thresholds of 4-7× baseline, some protocols yield PRP with lower platelet counts than whole blood [53, 64, 103]. Initially applied in hematology and later in surgery and dermatology, PRP is now used across multiple fields including plastic and reconstructive surgery [18, 57, 66, 90, 108, 133, 135].

In lipofilling, PRP's regenerative potential stems from its proangiogenic and anti-inflammatory effects. Early studies, including Rigotti et al. [25], observed enhanced vascular response and immune activation after PRP-enriched fat grafting, though improvements in regeneration were modest. Subsequent trials by Cervelli, Segreto, and Smith confirmed the safety and feasibility of PRP-enhanced fat grafting for wound healing, with some reporting accelerated healing and reduced pain [48]. However, randomized trials, such as Smith et al.'s diabetic foot ulcer study, found no significant clinical differences across groups, highlighting the need for larger studies.

Results remain mixed across applications. In facial atrophy (Fontdevila et al.), gluteal augmentation (Willemsen et al.), and scarring (Tenna et al.), PRP showed benefits in recovery and session reduction [7], while others, like Salgarello in breast reconstruction, found no added advantage [7]. Comparative studies with stromal vascular fraction (SVF) suggest both PRP and SVF enhance graft survival, though Gentile et al. reported superior outcomes with PRP in some contexts [9, 10, 125].

PRP contributes to fat graft viability by providing a fibrin matrix that supports adipocytes, suppresses inflammation, and retains growth factors. In vitro studies show that PRP enhances adipose-derived stem cell (ASC) proliferation, supports keratinocyte and fibroblast differentiation, and stimulates vascular network formation [48]. Additionally, PRP reduces preadipocyte apoptosis, suppresses inflammatory markers, and improves cell survival in co-cultures [36].

Optimal PRP concentration remains debated; 5-15% is generally beneficial, while higher levels (>40%) may be cytotoxic [68]. Although PRP enhances proliferation, high concentrations may inhibit adipogenic differentiation [14]. Nevertheless, PRP promotes ASC transdifferentiation into endothelial cells, crucial for angiogenesis [4].

Donor site selection also influences outcomes: abdominal and thigh fat – especially with thicker adipose layers – yields more viable ASCs and better graft retention [91].

Animal studies demonstrate that PRP-treated grafts show enhanced vascularization and fewer ischemic markers (e.g., vacuoles, oil cysts) within the first week post-injection [112, 126]. However, early revascularization is essential, as hypoxic adipocytes die within seven days. Activated PRP has demonstrated superior results over inactivated PRP or saline, with Hersant et al. reporting higher cell viability and vascular density [23, 112].

Although PRP improves the structural and vascular profile of fat grafts, the timeline of revascularization remains critical. If delayed, even PRP-induced angiogenesis may not prevent early ischemia-related cell loss.

CONCLUSION

This review provides an in-depth examination of the biological characteristics of adipose tissue and platelet-rich plasma (PRP), emphasizing their clinical relevance in plastic and reconstructive surgery. Adipose tissue, due to its abundance of multipotent stem cells, holds significant regenerative potential by supporting angiogenesis, immune modulation, and tissue regeneration. Advances in lipofilling – particularly through techniques like the Coleman method – have improved the reliability and consistency of fat grafting procedures. Nonetheless, challenges related to graft retention persist, highlighting the importance of complementary approaches to enhance graft integration and longevity.

PRP, recognized for its angiogenic and anti-inflammatory effects, has emerged as a promising adjuvant in fat grafting. A growing body of evidence supports the combined use of PRP and adipose tissue to improve graft viability, promote wound healing, and stimulate regenerative responses. In addition to enhancing vascularization, PRP facilitates stem cell differentiation, further strengthening its role in regenerative therapies. However, key challenges remain, including variability in PRP preparation techniques, uncertainty regarding optimal concentrations, and lack of standardized protocols for clinical application.

A central conclusion of this review is the need for continued investigation into the biological interplay between PRP and adipose tissue. Current findings suggest a synergistic interaction, but the underlying mechanisms require further clarification.

Limitations and future directions:

Current research is limited by the absence of standardized PRP preparation and delivery protocols, as well as a lack of long-term outcome data regarding fat graft survival. Future investigations should aim to establish unified guidelines that enhance the clinical efficacy of PRP and adipose tissue in regenerative procedures. Additionally, exploring the influence of donor site variability on graft quality and persistence, as well as defining optimal integration conditions for recipient tissues, will be critical for advancing clinical outcomes.

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ПЕРСПЕКТИВЫ ИСПОЛЬЗОВАНИЯ ОБОГАЩЕННОЙ ТРОМБОЦИТАМИ ПЛАЗМЫ И ПРОИЗВОДНЫХ ЖИРОВОЙ ТКАНИ В ХИРУРГИЧЕСКОЙ РЕГЕНЕРАТИВНОЙ МЕДИЦИНЕ

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Введение. Производные жировой ткани и плазма, обогащенная тромбоцитами (PRP), представляют собой перспективные средства регенеративной медицины и эстетической хирургии благодаря способности стимулировать восстановление тканей, усиливать ангиогенез и снижать воспаление. Их комбинированное применение активно внедряется в реконструктивной и пластической хирургии.

Цель. Оценить биологические функции и клинический потенциал производных жировой ткани и PRP в хирургии, особенно в контексте увеличения выживаемости жировых трансплантатов и регенерации тканей.

Проведён систематический обзор литературы с использованием баз данных *PubMed*, *Scopus* и *Web of Science* по протоколу PRISMA. Включались оригинальные исследования, обзоры и клинические испытания, посвящённые биологическим свойствам, механизмам действия и хирургическим результатам применения жировой ткани и PRP.

Жировая ткань содержит мультипотентные мезенхимальные стволовые клетки, способствующие ангиогенезу, иммуномодуляции и ремоделированию внеклеточного матрикса. PRP богат факторами роста, которые поддерживают клеточную пролиферацию, интеграцию трансплантата и контроль воспаления. Совместное использование PRP и жира улучшает приживление трансплантата и результаты заживления. Клинико-экспериментальные данные подтверждают улучшенные функциональные и эстетические результаты при реконструкции лица, заживлении ран и операциях на молочной железе.

Заключение. Комбинация PRP и жировых производных открывает значительные перспективы в хирургической регенеративной медицине. Однако разнообразие методов подготовки и применения затрудняет сравнение результатов. Необходимы дальнейшие исследования для стандартизации подходов и расширения клинического применения.

Ключевые слова: обогащенная тромбоцитами плазма; жировая ткань; регенеративная медицина; липофилинг; хирургия

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ХИРУРГИЯЛЫҚ РЕГЕНЕРАТИВТІ МЕДИЦИНАДА ТРОМБОЦИТТЕРГЕ БАЙ ПЛАЗМА МЕН МАЙ ТІНІНІҢ ӨНІМДЕРІН ҚОЛДАНУДЫҢ ЖАҢА МҮМКІНДІКТЕРІ

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Кіріспе. Май тіні мен тромбоциттерге бай плазма (PRP) регенеративті медицина мен эстетикалық хирургияда тіндердің қалпына келуін ынталандыру, ангиогенезді күшейту және қабынуды төмендету қабілетімен ерекшеленеді. Бұл компоненттердің біріктірілген қолданылуы пластикалық және реконструктивтік хирургияда белсенді түрде зерттелуде.

Мақсаты. Май тінінің туындылары мен PRP-нің хирургиялық қолданудағы биологиялық әсерлерін және клиникалық әлеуетін бағалау.

PubMed, *Scopus* және *Web of Science* дерекқорларынан PRISMA стандарттарына сәйкес жүйелі әдеби шолу жүргізілді. Қарауға бастапқы зерттеулер, шолулар және клиникалық зерттеулер енгізілді.

Май тінінде ангиогенезге, иммуномодуляцияға және матриксті қайта құруға ықпал ететін мезенхималық дің жасушалары бар. PRP жасушалық пролиферацияны, тіндік интеграцияны және қабынуды бақылауды қамтамасыз ететін өсу факторларына бай. PRP мен май трансплантатын бірлесіп қолдану трансплантаттың тіршілік етуін жақсартады. Клиникалық зерттеулер PRP қолданумен бет құрылымын қалпына келтіру, жараны емдеу және омырау хирургиясы кезінде функционалдық және эстетикалық нәтижелердің жақсарғанын көрсетеді.

Қорытынды. PRP және май тініне негізделген терапияларды біріктіру регенеративті хирургияда елеулі артықшылықтар береді. Алайда дайындау әдістерінің әртүрлілігі нәтижелерді салыстыруды қиындатады. Осы бағыттағы клиникалық қолдануды кеңейту үшін стандарттау мен қосымша зерттеулер қажет.

Кілт сөздер: тромбоциттерге бай плазма; май тіні; регенеративті медицина; липофилинг; хирургия