

## Stem Cell Therapy Applications in Surgical Wound Repair: A Qualitative Systematic Review

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### ABSTRACT

#### Background:

Stem cell therapy has emerged as a promising regenerative approach for enhancing surgical wound healing. Wound repair is a complex biological process involving inflammation, cell proliferation, angiogenesis, and tissue remodeling. However, various clinical conditions such as diabetes and vascular insufficiency may impair this process and lead to delayed healing.

#### Methods:

This qualitative systematic review aimed to explore the biological mechanisms, clinical applications, and translational challenges of stem cell therapy in surgical wound repair. A comprehensive literature search was conducted using PubMed, Scopus, and Web of Science databases. Priority was given to recent studies published from 2019 onward; however, seminal earlier studies were included where foundational mechanistic or regulatory relevance justified their inclusion.

#### Results:

The findings indicate that mesenchymal stem cells (MSCs) play a significant role in wound healing through immunomodulation, promotion of angiogenesis, and enhancement of extracellular matrix remodeling. Various delivery methods, including direct injection and biomaterial scaffolds, have shown promising outcomes. However, several challenges remain, including variability in stem cell sources, lack of standardized protocols, and regulatory limitations affecting clinical translation.

#### Conclusions:

Stem cell therapy demonstrates substantial potential in improving surgical wound healing and tissue regeneration. Despite encouraging results, further standardized clinical trials and regulatory frameworks are required to support widespread clinical application.

**Keywords:** Wound healing; Stem cells; Mesenchymal stem cells; Regenerative medicine; Tissue engineering; Surgical wound repair

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## 1. INTRODUCTION

The process of surgical wound repair is a highly coordinated biological process that helps to restore tissue integrity that has been injured or has undergone a surgical procedure. This is done through a series of overlapping stages such as inflammation, proliferation, and tissue remodeling. These phases are characterized by interactions of different types of cells, including fibroblasts, keratinocytes, endothelial cells, and immune cells using complex molecular signaling pathways to restore damaged tissue and rebuild skin integrity (Rodrigues et al., 2019; Tottali et al., 2020). In the usual physiological conditions, these processes guarantee effective repairing and recovery of the tissues functioning. Nevertheless, there are a number of systemic disorders that may interfere with the wound healing cascade and cause delayed wound healing or chronic wounds including diabetes mellitus, vascular disease and immune disorders (Guo & DiPietro, 2010).

Delayed wound healing is one of the major clinical problems in surgical practice and is linked to morbidity, longer hospital stay, and higher expenses in healthcare provision. The use of conventional treatment methods like wound dressings,

antibiotics, and surgical debridement has been unsuccessful in restoring the optimal regeneration of tissues in complex wounds. Consequently, regenerative medicine approaches that can stimulate the innate repair processes in the body and increase the clinical outcomes have begun to attract more attention (Garg et al., 2024).

The self-renewal and multipotent differentiation potential is some of the biological characteristics that have drawn significant interest into using stem cells in regenerative medicine. In particular, mesenchymal stem cells (MSCs) can be regarded as one of the most promising stem cell groups to be used in wound healing due to the possibility to regulate immune responses, release regenerative growth factors, and induce angiogenesis (Mahjoor et al., 2023). These cells are available in different types of tissues such as bone marrow, adipose tissue, umbilical cord blood, and placental tissues, hence can be relatively readily obtained and used in therapeutic procedures (Lopes et al., 2021).

Recent works indicate that therapeutic actions of MSCs are mostly realized by means of paracrine signaling and not by direct trans-differentiation into tissue-specific cells. The bioactive molecules released by MSCs are diverse (vascular endothelial growth factor (VEGF), transforming growth factor beta (TGF- $\beta$ ), and hepatocyte growth factor (HGF) and promote fibroblast proliferation, angiogenesis, and extracellular matrix remodeling (Farabi et al., 2024; Rodrigues et al., 2019). These processes increase tissue repair and speed up wound healing.

Additionally, tissue engineering has made it possible to develop new treatment methods that involve the combination of stem cells and biomaterial scaffolds to enhance the survival and incorporation of cells into damaged tissues. Scaffolds consist of biomaterials which offer mechanical support and the creation of an amenable microenvironment that improves stem cell performance and regenerative ability (Xiang et al., 2024; Tottoli et al., 2020). The above mentioned strategies have demonstrated encouraging outcomes in early clinical and preclinical research and there is a likelihood that stem cell based therapies would be a game changer in enhancing surgical wound healing.

Although these results are encouraging, there are still a number of issues that arise with being able to translate stem cell therapies into a standard clinical practice. Unpredictability of the stem cells origin, disparity in production processes, and regulatory challenges still restrain the extensive clinical use (Galipeau & Sensebé, 2018). Also, the variation in the study design and outcome measures in the clinical trials complicates the creation of standard therapeutic guidelines (Mitra et al., 2024).

Consequently, this qualitative systematic review will attempt to review the existing evidence of stem cell therapy in healing of surgical wounds. In particular, this review addresses three critical areas, including the biological processes that occur to ensure stem cell-mediated tissue regeneration, the clinical procedures and delivery methods that are applied in the management of wounds, and the barriers to translation that are relevant to the utilization of stem cell therapies in clinical procedures. Table 1 summarizes the primary sources of mesenchymal stem cells utilized in the applications of wound healing.

**Table 1. Major sources of mesenchymal stem cells (MSCs) and their regenerative roles in wound healing**

Stem Cell Source	Tissue Origin	Key Regenerative Functions	References
Bone marrow-derived MSCs	Bone marrow	Immunomodulation, angiogenesis, collagen synthesis	Farabi et al., 2024
Adipose-derived stem cells (ADSCs)	Adipose tissue	Rapid proliferation, secretion of growth factors	Mahjoor et al., 2023
Umbilical cord MSCs	Umbilical cord / Wharton's jelly	High regenerative potential and anti-inflammatory effects	Jin et al., 2023
Placental stem cells	Placental tissue	Enhanced tissue regeneration and immune regulation	Lopes et al., 2021

## 2. METHODS

The present study has assumed a qualitative systematic review approach to integrate the available evidence on the issue of the stem cell therapy in repairing surgical wounds. To achieve the research aim, a thorough literature search was carried out in leading scientific databases such as PubMed, Scopus, and Web of Science to find the peer-reviewed studies that explored the topic of stem cell-based therapies in wound healing.

Some keywords that were utilized in the search strategy were, stem cells, mesenchymal stem cells, wound healing, surgical wound repair, tissue regeneration, and regenerative medicine. The studies since 2019 were preferred to be used as the priority since, in this way, it is possible to speak about the latest achievements in the field of the research and regenerative

medicine.

The articles were selected based on the inclusion criterion of studies that investigated the biological underpinnings of stem cell-mediated healing, clinical trials of the use of stem cell therapy, or were articles discussing the challenges of translation in stem cell use in surgery. Experimental studies, as well as review articles were taken into consideration so as to present in detail the available scientific evidence.

The screening process of titles and abstracts was followed by the selection of relevant studies to analyze them in detail. Thematic synthesis then made it possible to analyze the included literature, and findings could be categorized into three key areas of analysis, namely, biological mechanisms of stem cell activity, clinical applications and delivery strategies, and qualitative analysis of translational barriers to integrating stem cell therapies into healthcare systems (Farabi et al., 2024; Díaz-García et al., 2021).

The selection of the studies was based on the guidelines of Preferred Reporting Items of Systematic Reviews and Meta-Analyses (PRISMA) (Page et al., 2021). In the initial analysis, 312 records were found in PubMed, Scopus, and Web of Science by conducting a comprehensive search of databases. The initial search result after elimination of the duplicate records (n= 72), yielded 240 articles to be screened in terms of titles and abstracts. After the screening process, 180 articles have been excluded because of being irrelevant to the stem cell therapy in wound healing of surgery. After that 60 articles were evaluated on eligibility, on a full text basis. Table 2 summarizes the features of the studies that were included in the qualitative synthesis.

**Table 2. Summary of the studies included in the qualitative synthesis**

Study	Study Type	Stem Cell Source / Focus	Application / Context	Key Findings
Othman & Tan, 2020	Review	Preconditioned stem cells	Regenerative therapy	Preconditioning methods increase the therapeutic efficacy, migration and survival of stem cells in regenerative medicine.
Díaz-García et al., 2021	Review	Skin stem cells	Skin regeneration and wound healing	The skin stem cells also facilitate the epidermal regeneration and assist in mechanisms of tissue repair.
El-Kadiry et al., 2021	Review	Stem cell-based therapies	Regenerative medicine	Due to its regenerative and immunomodulatory capabilities, stem cell therapies exhibit therapeutic potential in a wide range of diseases.
Farabi et al., 2024	Systematic review	Mesenchymal stem cells (MSCs)	Wound healing applications	MSC therapy enhances wound healing by angiogenesis, growth factor release and immune modulation.
Galipeau & Sensebé, 2018	Clinical review	Mesenchymal stromal cells	Clinical translation of cell therapy	The MSCs have issues with regulation, manufacturing and standardization to aid clinical application.
Garg et al., 2024	Review	Stem cells in wound repair	Tissue regeneration strategies	Stem cells enhance wound healing by paracrine signaling, angiogenesis and extracellular matrix remodelling.
Guo & DiPietro, 2010	Mechanistic review	Wound healing biology	Tissue repair mechanisms	The process of wound healing is a process of systemic coordinated inflammatory, proliferative and remodeling.
Ho et al., 2023	Review	Stem cell delivery systems	Diabetic wound therapy	Advanced delivery strategies improve stem cell survival, retention, and therapeutic outcomes
Jin et al., 2023	Review	Stem cells in regenerative medicine	Tissue repair and regeneration	Stem cells exhibit strong regenerative potential and are widely investigated for tissue engineering applications
Lopes et al., 2021	Review	Mesenchymal stem cells	Regenerative medicine applications	MSCs possess immunomodulatory, anti-inflammatory, and regenerative properties useful for tissue repair
Mahjoor et al., 2023	Experimental	Mesenchymal	Wound healing	MSCs enhance wound repair through

Study	Study Type	Stem Cell Source / Focus	Application / Context	Key Findings
	review	stromal cells	therapy	immune regulation, angiogenesis, and improved cellular microenvironment
Mitra et al., 2024	Experimental study	MSC-derived conditioned medium	Cellular regeneration	Stem cell-derived factors demonstrate cytoprotective and regenerative effects in epithelial cells
Nallakumarasamy et al., 2022	Review	MSC-derived extracellular vesicles	Regenerative wound healing	Extracellular vesicles derived from MSCs promote angiogenesis and fibroblast proliferation during wound repair
Rodrigues et al., 2019	Mechanistic review	Cellular mechanisms of wound healing	Tissue repair biology	Describes cellular and molecular mechanisms underlying wound healing processes
Tottoli et al., 2020	Review	Emerging wound healing therapies	Skin regeneration	Emerging biomaterials and regenerative approaches enhance wound healing outcomes
Xiang et al., 2024	Review	Stem cells with biological scaffolds	Tissue engineering for wound repair	Biomaterial scaffolds improve stem cell survival and promote tissue regeneration in wound healing

As shown in Figure 1, PRISMA 2020 flow diagram illustrating the study selection process for this systematic review. The study selection process followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines. A comprehensive database search identified 312 records from PubMed, Scopus, and Web of Science. After removal of 72 duplicate records, 240 studies underwent title and abstract screening. Of these, 180 records were excluded for irrelevance to stem cell therapy in surgical wound repair. Sixty full-text articles were assessed for eligibility, of which 44 were excluded due to non-surgical wound focus, absence of stem cell intervention, insufficient methodological reporting, or evaluation of non-wound clinical applications. Ultimately, 16 studies met the inclusion criteria and were included in the qualitative synthesis.

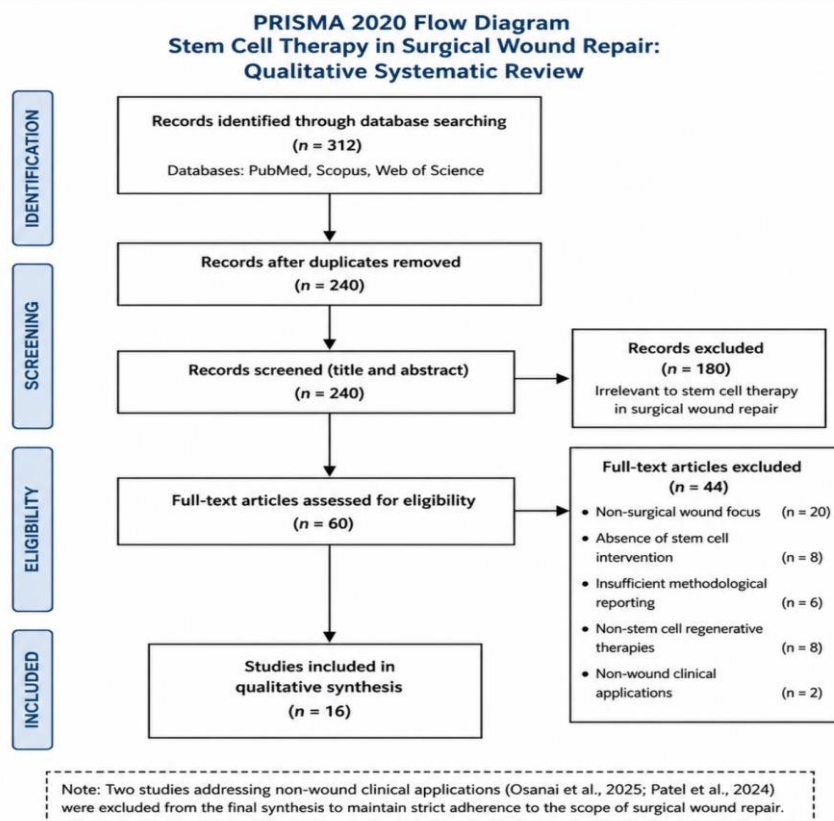


Figure 1. PRISMA 2020 flow diagram illustrating the study selection process for the qualitative systematic review of stem cell therapy in surgical wound repair.

### 3. BIOLOGICAL MECHANISMS OF STEM CELLS IN SURGICAL WOUND HEALING

#### 3.1 Phases of Surgical Wound Healing

The wound healing process is a highly controlled dynamic biological process that involves restoration of structural and functional integrity of damaged tissue. This is done in a number of overlapping steps which include inflammation, proliferation and tissue remodelling. At every stage, the concerted efforts of several cell types and signaling molecules are involved, which, collectively, leads to the healing process of the tissue (Rodrigues et al., 2019; Tottali et al., 2020).

The inflammatory process starts directly after tissue damage and includes platelet activation, as well as the formation of clots, which exclude excessive bleeding and offer a temporary scaffold in which cells migrate. In this phase, neutrophils and macrophages are brought to the wound and they eliminate debris and pathogens and release cytokines and growth factors that trigger the healing cascade (Guo & DiPietro, 2010). Though inflammation is essential in wound healing process, the chronic inflammatory process may result in poor tissue repair and can cause chronic wound.

After the inflammatory stage, a proliferative phase occurs which usually occurs a few days after the injury. In this phase, fibroblasts multiply and produce extracellular matrix, such as collagen and Fibronectin, which forms structural support to new tissue. At the same time, the process of angiogenesis takes place when new blood vessels are created by endothelial cells to replenish the oxygen and nutrient delivery to the regenerating tissue (Rodrigues et al., 2019). Keratinocytes also cross the wound surface to epithelialize the wound and replenish the epidermal reticulum.

The last phase of wound healing is the remodeling phase, which may take a number of months or even years. At this stage, the collagen fibers are restructured and cross-linked to make the tissue stronger and more stable. It is due to the fact that the fibroblasts and inflammatory cells are slowly eliminated by apoptosis leading to the mature scar tissue being formed (Rodrigues et al., 2019). These phases should be effectively regulated to achieve successful wound healing and when they are disturbed they can cause delay in wound healing or pathological scarring.

Stem cells are significant in supplementing these biological functions through the regulation of inflammation, angiogenesis-stimulant, and extracellular matrix remodelling. Such regenerative capabilities have exhibited stem cells as a key theme of research in regenerative medicine and wound healing therapies (Farabi et al., 2024).

#### 3.2 Mesenchymal Stem Cells and Immunomodulation

One of the most popular examples of stem cell populations used in regenerative medicine is mesenchymal stem cells (MSCs). These mesenchymal stromal cells are multipotent and can differentiate to various types of cells including osteoblasts, adipocytes and chondrocytes and can also regulate immune responses by secreting bioactive molecules (Lopes et al., 2021).

MSCs have one of the biggest therapeutic properties which is the regulation of the inflammatory process during wound healing. MSCs are known to communicate with diverse immune cells among them the T cells, macrophages as well as natural killer cells, to regulate the level of inflammation at the injured tissue site. MSCs may also remodel the polarization of macrophages between the pro-inflammatory M1 and the anti-inflammatory M2 phenotypes by releasing cytokines and immunomodulatory factors, thus decreasing the inflammation process and stimulating tissue regeneration (Mahjoor et al., 2023).

Besides modulating macrophages, MSCs release a number of immunoregulatory molecules, including prostaglandin E2, nitric oxide, and indoleamine 2,3-dioxygenase (IDO) which promote the inhibition of excessive immune reactions and repair tissue damages (Farabi et al., 2024). These immunomodulatory effects are useful especially in the chronic wounds where the inflammation process becomes persistent and suppresses natural healing.

Besides, the MSCs are able to dynamically react to the inflammatory signals within the wound microenvironment. MSCs increase their release of anti-inflammatory mediators when exposed to inflammatory cytokines interferon gamma and tumor necrosis factor alpha, which increases their therapeutic efficacies (Mitra et al., 2024). This form of adaptation enables MSCs to act as **dynamic regulators** of the wound healing process

#### 3.3 Angiogenesis and Tissue Regeneration

Angiogenesis, the development of new blood vessels out of existing blood vessels, is an important element of wound healing, as it guarantees sufficient oxygen supply, as well as nutrients, to the regenerating tissues. Angiogenesis impairment may cause tissue hypoxia and retarded tissue healing, especially in diabetic or vascular diseases patients (Guo & DiPietro, 2010).

Stem cells are important in enhancing angiogenesis by secreting angiogenic growth factors. Mesenchymal stem cell

secretes vascular endothelial growth factor (VEGF), fibroblast growth factor (FGF) and hepatocyte growth factor (HGF) that induce growth and migration of endothelial cells resulting in new blood vessels being generated in the wound bed (Rodrigues et al., 2019).

Besides facilitating angiogenesis, the stem cells increase tissue regeneration by inducing the growth and movements of the fibroblasts and the keratinocytes. The production of the extracellular matrix components and the restoration of the epithelial barrier, which is necessary to achieve a wound closure, are the functions of these cells (Farabi et al., 2024). Through the improvement of these regenerative activities, stem cell therapy can greatly speed up the recovery of surgical sites.

Stem cell-derived extracellular vesicles have also been noted as having an important role in wound healing as of lately. Proteins, microRNAs, and signaling molecules are found in these vesicles and they regulate cellular communication, and tissue regeneration. It was reported that stem cell-derived vesicles positively impact angiogenesis, inflammation, and fibroblast proliferation, which makes them good bait in regenerative medicine (Nallakumarasamy et al., 2022).

### 3.4 Extracellular Matrix Remodeling

ECM is an important component of tissue that is involved in preserving the tissue structure and offering mechanical support in wound healing. The process of ECM remodeling consists of the controlled deposition and degradation of structural proteins (collagen, elastin, and fibronectin), which, together, define the strength and integrity of the newly developed tissue (Rodrigues et al., 2019).

Stem cells take part in ECM remodelling by modulating fibroblast actions and collagen production. MSCs release the enzyme matrix metalloproteinases (MMPs) that break down the destroyed extracellular matrix components at the same time enhancing the formation of new collagen fibers. It is a regulated process that supports the normal remodeling of the tissues and avoids the excessive development of scars (Farabi et al., 2024).

Moreover, during the remodeling process, stem cells affect the arrangement and alignment of collagen fibers, which contributes to the increase of mechanical strength of healed tissue and positively influences functional recovery. They especially affect surgical wounds where the optimal tissue regeneration is needed to restore normal physiological functions (Mahjoor et al., 2023).

### 3.5 Limitations of Stem Cell Therapy

Although there is a bright therapeutic perspective in the healing of wounds associated with the use of stem cells, a number of constraints still exist. The variability of sources and biological properties of stem cells can become one of the biggest issues because it may result in an uneven therapeutic response in various studies (Galipeau & Sensebé, 2018).

The other limitation is the low survival rate of transplanted stem cells after their administration. The apoptosis of many stem cells or their inability to integrate into the host tissue occurs because of adverse microenvironmental factors, including hypoxia, inflammation, and oxidative stress (Othman and Tan, 2020). Such difficulties have forced scientists to consider the possible solutions like biomaterial scaffolds and cell preconditioning to enhance the survival and treatment efficacy of the stem cells.

Also, legal and moral factors still affect the clinical progress of stem cell therapies. The disparities in regulatory systems of different states and the absence of standardized production guidelines have impeded the process of stem cell therapies turning into the standard clinical practice (Mitra et al., 2024).

## 4. CLINICAL APPLICATIONS OF STEM CELLS IN SURGICAL WOUND REPAIR

### 4.1 Clinical Burden of Surgical Wound Complications

This is because surgical wound complications are a major problem in the contemporary health systems. The complication can include infection, wound dehiscence, slow epithelialization, and persistent inflammation, which can seriously affect the postoperative recovery and make healthcare costs more significant. These complications seem to be prevalent in high-risk groups of patients such as patients with diabetes mellitus, obesity, vascular insufficiency and immunosuppressive conditions (Guo & DiPietro, 2010).

Late wound healing not only extends a hospital stay, but also, it predisposes to second-order infections as well as further surgery. Traditional methods of treatment such as wound dressing, antibiotic and surgical debridement are not usually adequate in encouraging the best tissue growth in complex wounds. Consequently, stem cell therapy and various other approaches to regenerative medicine have become the more and more popular alternatives to repairing wounds and achieving better clinical outcomes (Garg et al., 2024).

Clinical research studies have recently shown that the stem cell-based therapies have a high potential to restore

inflammatory complications, wound closure, and tissue regeneration. These therapeutic consequences are also explained mainly by the regenerative potential of stem cells, which comprise immunomodulation, the release of growth factors, and angiogenic stimulation (Farabi et al., 2024).

#### 4.2 Stem Cell Delivery Strategies

The success of the stem cell therapy greatly relies on the mode of cell delivery to the injured tissues. A number of delivery models have been formulated to improve survival, retention and curative efficacy of stem cells in the wound location.

Direct injection is one of the most simplest methods, whereby the stem cells are directly injected into the wound bed or the immediate tissue. The technique enables local delivery of therapeutic cells and is fairly simple to conduct in the clinical environment. Nevertheless, direct injection can lead to low cell viability rates caused by mechanical forces and unfavorable inflammatory conditions in damaged tissues (Ho et al., 2023).

The second research opportunity is the application of biomaterial scaffolds in order to deliver stem cells. Biomaterial scaffolds offer mechanical strength to the transplanted cells and offer a conducive microenvironment which improves cell survival and incorporation into the host tissues. They can be biodegradable (collagen, hydrogels, synthetic polymers that imitate the natural extracellular matrix, etc.) or non-biodegradable scaffolds (Tottoli et al., 2020; Xiang et al., 2024).

Delivery systems based on hydrogel have also been used in regenerative medicine. The hydrogels are able to entrap the stem cells and shield them against mechanical stress and release therapeutic factors into the wound conditions in a gradual manner. It has been demonstrated that hydrogel-based systems are much more effective in trapping stem cells, which leads to a more effective restoration of tissues than usual delivery techniques (Tottoli et al., 2020).

#### 4.3 Autologous Versus Allogeneic Stem Cells

A major issue that arises in the stem cell therapy is the option between autologous and allogeneic stem cells. Autologous stem cells are those that are taken out of the tissues of the patient, and allogeneic stem cells are obtained by the donors.

There are a number of benefits that autologous stem cells have, such as less chance of the patient developing immune rejection and better compatibility with the host tissue. These cells may be obtained out of bone marrow, adipose tissues or peripheral blood and are reintroduced to the patient once processed. Nevertheless, patient age, underlying medical conditions, and the time needed to produce cells in the laboratory could all be barriers to autologous stem cell therapy (Lopes et al., 2021).

On the contrary, allogeneic stem cells offer a more scalable treatment alternative due to the ability to prepare them in advance and store their use in medicine. The so-called healthy donors provide the cells that are usually produced in high numbers and which can be used in therapeutic procedures. Nonetheless, the application of allogeneic stem cells is associated with the issues of immune compliance, regulatory acceptance, and ethics (Galipeau & Sensebé, 2018).

Although such difficulties exist, in wound healing and tissue regeneration trials, both the autologous and allogeneic stem cell therapies have shown encouraging outcomes in clinical trials.

#### 4.4 Clinical Outcomes of Stem Cell Therapy

A number of clinical trials have recorded positive results regarding stem cell-based treatment of wounds. These researches have shown the enhancement of wound healing, scarring, and tissue regeneration in patients with the application of stem cell therapy (Farabi et al., 2024).

Stimulation of angiogenesis is one of the major ways in which the stem cells enhance the wound healing. The stem cells stimulate the development of new blood vessels and, as a result, increase oxygen and nutrient delivery to the injured tissue by secretion of angiogenic growth factors including VEGF and fibroblast growth factor (Rodrigues et al., 2019). Better vascularization is especially pertinent in chronic wounds where the tissue circulation is commonly impaired.

Remodeling and reduction of inflammation have also been observed to be possible through stem cell therapy. The stem cells suppress the action of immune cells and suppress the synthesis of inflammatory cytokines that may disrupt healing through immunomodulatory processes (Mahjoor et al., 2023). This is an effect that leads to a more positive healing environment and that promotes the regeneration of normal tissue.

Moreover, stem cells can enhance healed tissue quality because they can develop a well-organized collagen deposition and decrease scar excess. Such effects are especially useful in a surgical wound when the highest cosmetic and functional results are required (Farabi et al., 2024).

Although such promising results have been achieved, there is still inconsistency in clinical outcomes of studies in relation to varied sources of stem cells, modes of delivery, use of a dose, and patient groups. In its turn, this fact presupposes additional studies that will allow developing uniform treatment regimens that could guarantee uniform clinical results (Mitra et al., 2024).

## 5. QUALITATIVE SYNTHESIS: TRANSLATIONAL BARRIERS AND CONTEXTUAL INFLUENCES

### 5.1 Rationale for Qualitative Evidence Integration

Even though many quantitative studies have proven the regenerative nature of the stem cells in wound healing, the quantitative results are not enough to comprehend the complexity involved in applying the stem cell therapies into clinical practice. The clinical translation of regenerative medicine technologies is usually associated with a number of contextual elements such as institutional infrastructure, expertise of clinicians, regulatory frameworks, and ethical issues. Thus, qualitative synthesis is significant in the combination of evidence based on various research viewpoints and highly important identification of major challenges that affect therapeutic application (Mitra et al., 2024).

Qualitative systematic reviews enable the researcher to investigate tendencies involving numerous studies and determine common themes in the area of the adoption and clinical translation of new therapeutic options. Qualitative synthesis can be utilized in the context of surgical wound healing with stem cell therapy as it is possible to describe why potentially effective biological therapies can have some difficulties when entering clinical practice despite good preclinical results (El-Kadiry et al., 2021).

### 5.2 Translational and Regulatory Barriers

Among the significant issues connected to stem cell therapy, there is the complicated regulatory environment of the process of creating and using cell-based therapies. Approving new kinds of regenerative medicine treatments is a long process that requires a lot of safety and efficacy data by regulatory agencies like the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA). These control provisions are necessary to safeguard patient safety, yet they are capable of greatly hindering the process of converting promising therapies into the clinical setting (Galipeau & Sensebé, 2018).

The other significant obstacle is the absence of standard manufacturing guidelines on the production of stem cells. Stem cells may be obtained through several sources of tissues such as bone marrow, adipose tissue and umbilical cord blood, along with any variations in isolation protocol, culture protocol and expansion procedures could modify the biological properties of the cells. This inconsistency may lead to differences in the treatment outcomes of clinical studies (Farabi et al., 2024).

There is also the ethical consideration involved in the clinical development of the stem cell therapies. Even though the source of mesenchymal stem cells as the adult tissues is regarded as ethically acceptable, the issue of other sources of stem cells like embryonic stem cells are still controversial in most countries. Such ethical discussions may have a role in determining how research is financed, whether it advances to regulation or not, and how the community received the results of stem cell-based interventions (Garg et al., 2024).

### 5.3 Institutional and Infrastructure Challenges

The availability of specific infrastructure and technical expertise in healthcare institutions also determines the success of the implementation of stem cell therapies. Stem cell-based therapies commonly involve the use of sophisticated laboratory equipment to isolate and expand and quality control of cells. These complicated procedures might not be available in many healthcare systems, especially in countries with low- and middle-income levels, due to the lack of the necessary infrastructure (Mitra et al., 2024).

Moreover, clinicians will have to be trained specifically on the methods of regenerative medicine so that they can have the capacity to incorporate stem cell therapies in their surgical practice. Healthcare providers might remain hesitant to use new regenerative strategies without proper training and standardized treatment guidelines even when their clinical evidence indicates their potential effectiveness (Díaz-García et al., 2021).

Monetary issues are also one of the biggest obstacles in embracing stem cell therapies. Isolating the stem cells, culturing the cells, and the processing of the cells in the lab can be very expensive compared to the traditional wound care methods. Consequently, the healthcare systems can experience difficulties to integrate such therapies into the daily clinical practice because the long-term cost-effectiveness is not evident (Garg et al., 2024).

#### 5.4 Emerging Innovations and Future Directions

Nonetheless, some emerging technological developments can be used to address some of the barriers present, and enhance the clinical translation of stem cell therapies. The field of biomaterials and tissue engineering has allowed the creation of highly complex scaffold models that can promote better stem cell survival and regenerative success (Tottali et al., 2020).

Also, the recent advances in single cell transcriptomics have enabled scientists to establish particular stem cell subpopulations that can be more regenerative. It could be possible to increase predictability of therapeutic consistency and more confident clinical outcomes by choosing highly potent populations of stem cells (Díaz-García et al., 2021).

The other potential field of study is the application of extracellular vesicles derived using stem cells. Within these vesicles there are signaling molecules that can be used to stimulate tissue regeneration without necessarily having to transplant actual cells. This method can help mitigate some of the safety issues related to stem cell therapy and at the same time have regenerative effects (Nallakumarasamy et al., 2022).

## 6. DISCUSSION

The results of this qualitative systematic review indicate that stem cell therapy has an enormous potential in terms of regenerative process to enhance the healing of a surgical wound. Stem cells, most notably mesenchymal stem cells, have several therapeutic functions such immunomodulation, angiogenesis stimulation, and remodelling of extracellular matrix. The summing up of these mechanisms leads to a better healing of the wounds and enhanced tissue regeneration (Farabi et al., 2024).

Experimental and clinical evidence shows that stem cell-based therapy can facilitate wound healing and enhance the quality of tissue in patients with complicated wounds. Regulatory nature of inflammatory responses and vascularization of stem cells is instrumental in the restoration of tissue functions and inhibition of the formation of chronic wounds (Rodrigues et al., 2019).

Nevertheless, even though preclinical research has shown positive outcomes, a number of obstacles still hinder the extensive clinical use of stem cell therapy. The variability of sources of stem cell, disparities in methods of cell processing, and control issues continue to be significant barriers to the standardization of regenerative treatments (Galipeau & Sensebé, 2018).

The other issue of concern is the low survival rate of transplanted stem cells through hostile wound conditions that are inflammatory, hypoxic, and oxidative. Biomaterial scaffolds, hydrogel delivery, and prescriptions are some of the strategies being explored to enhance the survival and therapeutic efficacy of stem cells (Othman and Tan, 2020).

In future research directions, there is a need to seek ways of coming up with uniform guidelines on the isolation, growth, and delivery of stem cells, in order to achieve standardized clinical results. Also, investigations on the safety, efficacy, and long-term advantages of the stem cell-based therapies in managing surgical wounds require large-scaled randomized clinical trials.

In spite of the overall synthesis in this review, there are some limitations that need to be identified. First, the review has been based mainly on the already published research that could predispose it to publication bias. Second, the disparity in study design, the sources of the stem cells, and the treatment regimen in the studies included has the ability to influence the generalizability of the results. Lastly, a lot of research is in the preclinical phase and thus more large-scale randomized clinical trials are required to ascertain the clinical efficacy and safety of stem cell-based therapies in repairing surgical wounds.

## 7. CONCLUSION

Stem cell therapy is an emerging technology that can be used to improve the healing of a surgical wound and regenerative medicine. Mesenchymal stem cells also have specific biological characteristics that allow them to control inflammation, facilitate angiogenesis, and facilitate remodeling of the extracellular matrix during recovery of wounds. These healing properties render the stem cell therapy an effective treatment option to enhance recovery in patients that have complicated surgical wounds.

Even with this advancement in the field of stem cell studies, there are still numerous obstacles that prevent the clinical application of such treatments. Complexity of regulations, differences in sources of stem cells, and absence of uniform treatment regimens are still significant impediments to large-scale clinical adoption.

Subsequent developments in tissue engineering, biomaterials, and targeted cell choice can potentially address these issues and enhance the therapeutic value of stem cell-based therapies. As interdisciplinary research and cooperation between scientists, clinicians, and regulatory agencies continues, in the future stem cell therapy can be a part and parcel of contemporary management of surgical wounds.

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