Research Article

Evidence-Based Role Of Stem Cell Therapy In Perioperative Care – A Scientific Analysis

D .Merbin Farrisa[1], P.Krubaa[2],S Parthasarathy[3]

[1]Junior Resident, Department of anaesthesiology, Mahatma Gandhi Medical college and Research Institute, Sri Balaji Vidyapeeth, Pondicherry, India 607402
[2]Department of Biotechnology, Periyar Maniammai Institute of Science & Technology,(deemed to be university) Vallam, Thanjavur, India
[3.] Professor, Department of anaesthesiology Mahatma Gandhi Medical college and Research Institute, Sri Balaji Vidyapeeth, Pondicherry, India 607402
[1]Corresponding author email id: merfy29@gmail.com

Abstract

Stem cell therapy has emerged as a promising adjunct in perioperative care due to its potent immunomodulatory, anti-inflammatory, and regenerative properties. Mesenchymal stem cells (MSCs) and bone marrow–derived stem cells (BMSCs) function as "medicinal signaling cells," exerting therapeutic effects through paracrine mechanisms, including cytokine secretion, angiogenesis promotion, and immune regulation. Evidence from randomized controlled trials and systematic reviews demonstrates that intramyocardial transplantation of autologous BMSCs during coronary artery bypass grafting significantly improves left ventricular ejection fraction in patients with ischemic heart disease and congestive heart failure, representing the strongest clinical support for perioperative stem cell application.

In orthopedic surgery, clinical trials and systematic reviews suggest that MSCs and bone marrow aspirate concentrate enhance fracture healing, reduce inflammation, and improve functional recovery following joint replacement and tendon repair procedures. However, substantial heterogeneity in study design, cell source, dosing, and outcome measures limits definitive conclusions. Evidence also supports the role of stem cells in reducing postoperative fibrosis, scar formation, and pain by modulating inflammatory pathways and promoting physiological tissue regeneration.

Experimental and clinical studies indicate potential benefits in organ-related surgeries, including liver regeneration and cardiac repair. Major barriers to widespread clinical adoption include variability in harvesting techniques, processing protocols, delivery routes, and cell dosage, resulting in inconsistent therapeutic outcomes across studies.

In conclusion, stem cell therapy demonstrates significant potential to enhance perioperative recovery by reducing inflammation, accelerating tissue repair, and improving functional outcomes. Standardized protocols and large-scale randomized controlled trials are essential to establish long-term safety, efficacy, and cost-effectiveness before routine clinical implementation.

Keywords: Stem Cells; Perioperative Care; Tissue Regeneration; Postoperative Complications.

INTRODUCTION:

Stem cells have the remarkable potential to renew themselves. They can develop into many different cell types in the body during early life and growth. Stem cells are endorsed with indefinite cell division potential, can transdifferentiate into other types of cells, and have emerged as frontline regenerative medicine source in recent time, for reparation of tissues and organs anomalies occurring due to congenital defects, disease, and age associated effects.

Advances in regenerative medicine have introduced new therapeutic approaches aimed at improving tissue repair and functional recovery following injury or disease. Stem cell therapy has gained considerable attention in recent decades due to its ability to regenerate damaged tissues and modulate immune responses. Stem cells are undifferentiated cells characterized by their capacity for self-renewal and differentiation into specialized cell types. These unique properties make them valuable for therapeutic applications in various medical fields, including cardiology, orthopaedics, neurology, and surgery.

The perioperative period represents a critical phase in patient management, during which surgical trauma, anaesthesia, and physiological stress responses may lead to inflammation, tissue damage, and organ dysfunction.

Postoperative complications such as delayed wound healing, infections, organ injury, and prolonged recovery remain major concerns in surgical practice.

Stem cell therapy offers a novel strategy to address these limitations by enhancing the body's intrinsic healing mechanisms. Experimental studies have demonstrated that stem cells can promote angiogenesis, reduce inflammation, and stimulate tissue regeneration through both direct differentiation and paracrine signaling mechanisms. In particular, mesenchymal stem cells have shown promising potential in improving postoperative outcomes due to their anti-inflammatory and immunomodulatory properties.

In recent years, increasing research has explored the role of stem cell therapy in perioperative medicine. These studies suggest potential benefits in areas such as wound healing, surgical flap survival, bone regeneration, and protection against organ injury. However, despite encouraging findings, the integration of stem cell therapy into routine perioperative care remains limited.

This article aims to critically analyze the current evidence regarding the role of stem cell therapy in perioperative care, with particular emphasis on mechanisms of action, clinical applications, implications for anaesthetic practice, and future research directions.[1-5]

Methodology:

This narrative review was conducted through a comprehensive literature search of PubMed/MEDLINE, Scopus, Web of Science, and Google Scholar to identify relevant studies on stem cell therapy in perioperative medicine. The search included articles published from January 2010 to June 2026. The primary search terms included "stem cell therapy," "mesenchymal stem cells," "bone marrow-derived stem cells," "perioperative care," "anaesthesia," "regenerative medicine," "wound healing," "organ protection," "cardiac surgery," "orthopaedic surgery," and "postoperative recovery." Boolean operators (AND/OR) were used to refine the search.

Original research articles, randomized controlled trials, systematic reviews, meta-analyses, and relevant clinical guidelines published in English were considered. Experimental studies with significant translational relevance were also included where clinical evidence was limited. Conference abstracts, editorials, duplicate publications, and studies lacking adequate methodological details were excluded. Priority was given to high-quality evidence, particularly systematic reviews, meta-analyses, and randomized controlled trials, to provide a balanced overview of the current evidence supporting stem cell therapy in perioperative medicine.

Types of Stem Cells Used in Perioperative Medicine:

Stem cells are broadly classified based on their origin and differentiation potential.[6]

Stem cells can be:

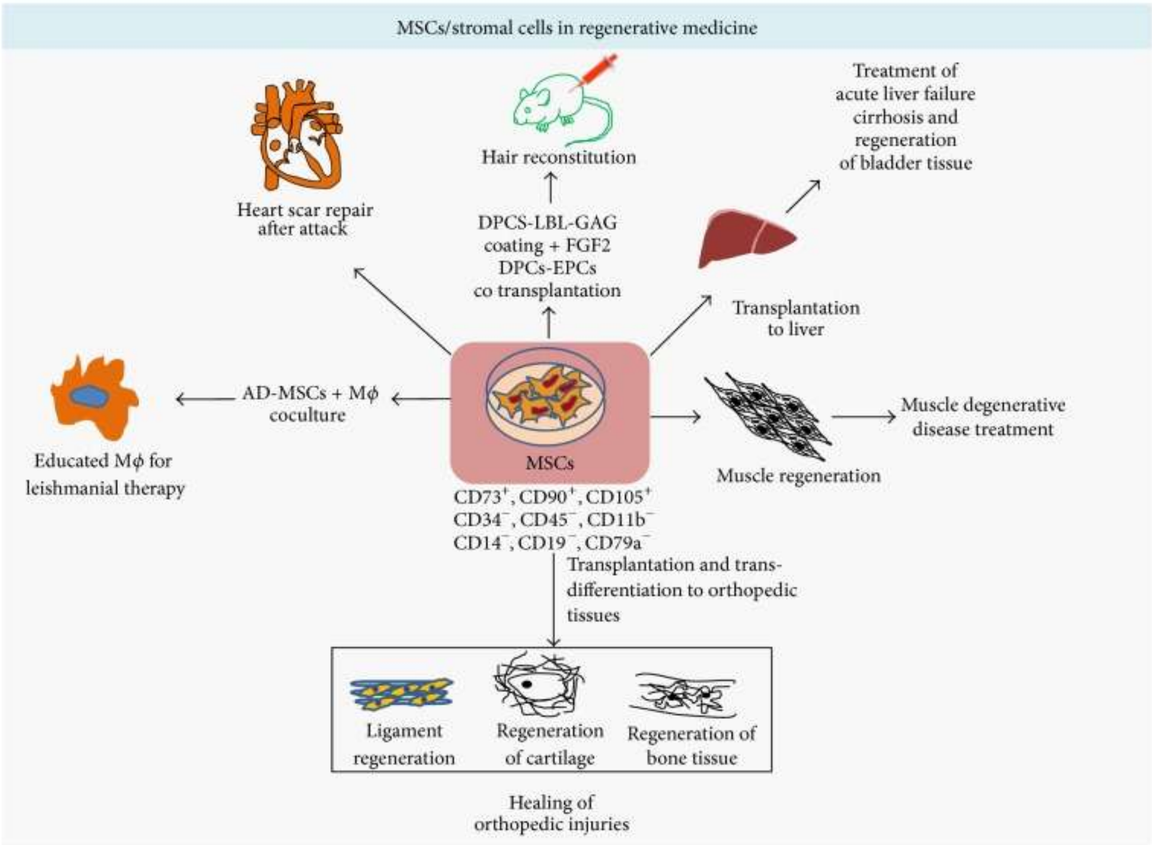
(i) totipotent, such as the ones of the zygote, which can give rise to any cell in an organism and to extraembryonic structures;
(ii) pluripotent, such as embryonic cells that can differentiate into any cell in the germ layers;
(iii) multipotent if they can differentiate into different cell types within specific lineages, such as hematopoietic stem cells;
(iv) oligopotent, with the capacity to differentiate into only some cell types; and
(v) unipotent, which gives rise to a specific cell type.

On the basis of regenerative applications, stem cells can be categorized as embryonic stem cells (ESCs), tissue specific progenitor stem cells (TSPSCs), mesenchymal stem cells (MSCs), umbilical cord stem cells (UCSCs), bone marrow stem cells (BMSCs), and iPSCs

- Embryonic Stem Cells: ESCs, sourced from ICM of gastrula, have tremendous promises in regenerative medicine. These cells can differentiate into more than 200 types of cells representing three germ layers. With defined culture conditions, ESCs can be transformed into hepatocytes, retinal ganglion cells, chondrocytes, pancreatic progenitor cells, cone cells, cardiomyocytes, pacemaker cells, eggs, and sperms which can be used in regeneration of tissue and treatment of disease in tissue specific manner.
- Tissue specific stem and progenitor cells: TSPSCs have potential to differentiate into other cells of the tissue. Characteristically inner ear stem cells can be transformed into auditory hair cells, skin progenitors into vascular smooth muscle cells, mesoangioblasts into tibialis anterior muscles, and dental pulp stem cells into serotonin cells. Transplantation of TSPSCs regenerates targets tissue such as regeneration of tibialis muscles from mesoangioblasts, cardiac tissue from AdSCs, and corneal tissue from limbal stem cells. Cell growth and transformation factors secreted by TSPSCs can change cells fate to become other types of cell, such that SSCs coculture with skin, prostate, and intestine mesenchyme transform these cells from MSCs into epithelial cells fate

- Mesenchymal Stem Cells: MSCs are CD73+, CD90+, CD105+, CD34−, CD45−, CD11b−, CD14−, CD19−, and CD79a− cells, also known as stromal cells. These bodily MSCs represented here do not account for MSCs of bone marrow and umbilical cord. Upon transplantation and transdifferentiation these bodily MSCs regenerate into cartilage, bones, and muscles tissue. Heart scar formed after heart attack and liver cirrhosis can be treated from MSCs. Most commonly used clinically. These cells possess several properties that make them suitable for clinical use, including low immunogenicity, immunomodulatory effects, and the ability to secrete bioactive molecules that promote tissue repair. Mesenchymal stem cells are currently the most widely investigated in perioperative research due to their safety profile and regenerative capabilities.

Sources: Bone marrow, Adipose tissue, Umbilical cord.



- Umbilical cord stem cells: UCSCs, the readily available source of stem cells, has emerged as futuristic source for personalized stem cell therapy.
- Bone marrow stem cells: bone marrow, the soft sponge bone tissue that consisted of stromal, hematopoietic, and mesenchymal and progenitor stem cells, is responsible for blood formation. Even halo-HLA matched BMSCs can cure from disease and regenerate tissue. BMSCs can regenerate craniofacial tissue, brain tissue, diaphragm tissue, and liver tissue and restore erectile function and transdifferentiation monocytes.
- Induced pluripotent stem cells: using the edge of iPSCs technology, skin fibroblasts and other adult tissues derived, terminally differentiated cells can be transformed into ESCs-like cells. It is possible that adult cells can be transformed into cells of distinct lineages bypassing the phase of pluripotency. The tissue specific defined culture can transform skin cells to become trophoblast, heart valve cells, photoreceptor cells, immune cells, melanocytes, and so forth. ECM complexation with iPSCs enables generation of tissue organoids for lung, kidney, brain, and other organs of the body. Similar to ESCs, iPSCs also can be transformed into cells representing three germ layers. \

Mechanisms of Action in Perioperative Care:

1. Immunomodulation
MSCs can modulate immune responses, by reducing cytokines such as TNF-α and IL-6 and creating a supportive environment for tissue repair, thereby suppresses excessive inflammation
2. Angiogenesis
They stimulate vascular growth by releasing growth factors.
Example:VEGF, FGF, PDGF
Studies show stem cell therapy enhances angiogenesis and increases vascular density in surgical tissues.
3. Tissue regeneration by Differentiation and Cell Replacement:
Stem cells can differentiate into specific cell types (e.g., cardiomyocytes, neurons) to replace damaged or dead cells, restoring tissue function.
4. Anti-fibrotic effects
Reduce scar formation and fibrosis.
5. Paracrine signaling (Trophic Effects): Rather than just replacing cells, stem cells often act by secreting bioactive molecules (cytokines, chemokines, and growth factors) that create a regenerative microenvironment.
6. Exosome/Microvesicle Transfer: Stem cells release exosomes, which are small vesicles that transfer proteins, lipids, and genetic material to injured cells, promoting survival and regeneration.
7. Mitochondrial Transfer: In cases of tissue ischemia, stem cells can transfer functional mitochondria to damaged cells via tunneling nanotubes, rescuing them from apoptosis.

Evidence-Based Applications in Perioperative Care:

Cardiothoracic surgery:
Intramyocardial transplantation of stem cells in CABG – Improves LVEF
Adult stem cells treatment in IHD and CHF- Improves LVEF, Potential benefit in terms of mortality in the long term.
Intracoronary stem cell injection after MI- Short term benefits.
Treatment of acute lung injury and acute respiratory distress syndrome- Vascular regeneration.
Tissue engineered heart valve from MSC, fibroblasts - Revolutionize cardiac surgery in the future.
General surgery:
To prevent or minimize the development of post surgical scars by intradermal injection of stem cells – significant potential in the enhancement of cutaneous healing.
Injection of stem cells with fibrin glue – for management of perianal fistula.
Though there are limited clinical evidence Stem cell can also be used in management of hepatic disease- hepatic regeneration, matrix remodeling, hepatocyte differentiation.
Neurosurgery:
Hematopoietic stem cells – partially resolve gastrointestinal, muscular and cerebral manifestations of neuromuscular diseases.
Umbilical cord mesenchymal stem cell – improves neurological condition in patients with sequelae of TBI.
Intraarterial injection of stem cell- treatment of spinal cord injury.
Allogenic umbilical cord blood stem cells- improve motor and cognitive function of people with cerebral palsy.
Paediatric surgery:
Correction of cleft palate – application of stem cell to engineered palate.
HDCT followed by stem cell transplantation for childhood medulloblastoma- provide long term survival.
Orthopaedic surgery:
Stem cells with growth factors- promote healing in non- union and delayed fracture.
MSC in intervertebral disc chondrocytes- lumbar disc disease
Intraarticular injection- degenerative orthopedic pathologies- osteoarthritis, tendinopathies.
Intraarticular injection pf stem cells- augments meniscus repair and replacement, ant. Cruciate ligament reconstruction or repair.
MSC- Rotator cuff repair.
Plastic surgery:
Stem cell enriched tissue injections- soft tissue augmentation and regeneration, non- healing wound healing, bone reconstruction.
Intra-op use of adult stem cell – in oral reconstructive surgery.
ENT surgery:

Stem cell enriched tissue injections- soft tissue augmentation and regeneration, non- healing wound healing, bone reconstruction.
Intra-op use of adult stem cell – in oral reconstructive surgery.

Vascular surgery:

Intramuscular infusion- for treatment of limb ischemia.
Intramuscular injections of stem cells into the threatened limb- critical limb ischemia treatment.r surgery.

Urology:

USG guided transurethral injections of myoblasts and fibroblasts- regeneration of damaged sphincter components in the treatment of urinary incontinence.
Pluripotent stem cells used for construction of kidney tissue.
ESC, amniotic fluid derived stem cell for bladder regeneration, repair of urinary tract injury- future of reconstructive surgeries.
Bone marrow derived MSC- reduce acute rejection in patients with ESRD who undergoes ABO compatible cross match- negative kidney transplants from a living related donor -lower incidence of acute rejections, decreased risk of opportunistic infection and better renal function at 1 year.

Organ Protection:

Stem cells have been investigated in:

- lung injury
- kidney injury
- cardiac ischemia

Key mechanisms of action across these conditions include:

1. Immunomodulation and Anti-inflammation
   - ✓ Macrophage Repolarization: Stem cells, particularly MSCs, shift macrophages from a pro-inflammatory M1 phenotype to an anti-inflammatory M2 phenotype.
   - ✓ Cytokine Regulation: They secrete anti-inflammatory mediators such as interleukin-10 (IL-10), transforming growth factor-β (TGF-β), and prostaglandin E2 (PGE2) while suppressing pro-inflammatory cytokines like TNF-α and IL-6.
   - ✓ T-Cell Suppression: MSCs inhibit the proliferation and activation of T-helper 1 (Th1) and Th17 cells, which reduces immune-mediated damage in sepsis and inflammatory states.
2. Anti-Apoptotic and Pro-Survival Effects
   - ✓ Modulating Survival Pathways: MSCs upregulate anti-apoptotic genes (e.g., Bcl-2, Bcl-xL) and downregulate pro-apoptotic genes (e.g., Bax, caspase-3) in damaged cells.
   - ✓ Promoting Regeneration: In AKI and lung injury, MSCs release trophic factors like HGF (hepatocyte growth factor), IGF-1, and VEGF that stimulate endogenous cell proliferation.
3. Anti-Oxidative Stress
   - ✓ Upregulating Antioxidants: Stem cells induce the expression of antioxidant enzymes such as Heme Oxygenase-1 (HO-1), which reduces Reactive Oxygen Species (ROS) accumulation and mitochondrial dysfunction.
   - ✓ Scavenging ROS: MSC-derived exosomes have been shown to reduce ROS accumulation by enhancing the scavenging capacity of injured tissues.
4. Paracrine Signaling and Extracellular Vesicles (EVs)
   - ✓ Micro vesicle (MV) Delivery: MSCs release EVs (exosomes and microvesicles) that carry proteins, miRNAs, and mRNAs to injured cells.
   - ✓ RNA Transfer: These vesicles deliver genetic information (e.g., miRNA-30, miRNA-146b) that regulates post-transcriptional gene expression to inhibit apoptosis and reduce fibrosis.

Organ-Specific Actions:
AKI: They promote renal tubular cell proliferation and reduce tubular necrosis.
Lung Injury (ALI/ARDS): MSCs secrete Keratinocyte Growth Factor (KGF), which improves alveolar fluid clearance and endothelial stability (Angiopoietin-1).
Trauma: Stem cells modulate excessive inflammation at the injury site and promote angiogenesis to restore blood supply.
Surgery: In cardiac surgery, MSCs have been shown to provide a protective, non-tumorigenic effect, reducing the risk of postoperative AKI.

5. Homing Ability

- ✓ Targeted Migration: Stem cells possess a natural ability to "home" to sites of damage, driven by chemical signals (chemokines) released by inflamed or injured tissues, such as the CXCL12/CXCR4 axis

These mechanisms may reduce postoperative complications such as:

- sepsis
- inflammatory organ injury.

Anaesthetic Implications:

The use of stem cell therapy in perioperative medicine has important implications for anaesthesiologists.

First, understanding the timing and route of stem cell administration is essential for optimizing therapeutic effects. Stem cells may be administered preoperatively, intraoperatively, or postoperatively depending on the clinical indication.

Second, anaesthetic drugs and perioperative medications may influence stem cell viability and function. For example, certain anesthetic agents may alter cellular metabolism and inflammatory responses, potentially affecting stem cell activity.

Third, stem cell therapy may reduce postoperative inflammation and improve tissue perfusion, which could influence anesthetic management and postoperative recovery.

Anaesthesiologists must also consider potential risks associated with stem cell therapy, including immune reactions, infection transmission, managing potential adverse reactions like pulmonary embolism or graft rejection and tumor formation. Close monitoring and multidisciplinary collaboration are essential when integrating stem cell therapies into perioperative care.

Limitations and Ethical Considerations:

Despite promising results, several limitations hinder the widespread adoption of stem cell therapy in perioperative medicine.

One major limitation is the lack of large randomized controlled trials evaluating the safety and efficacy of stem cell therapy in surgical patients. Most available studies are experimental or early-phase clinical trials.

Ethical concerns also arise with the use of embryonic stem cells due to issues related to embryo destruction. Although adult stem cells and induced pluripotent stem cells address some of these concerns, regulatory frameworks continue to evolve.

Additionally, stem cell therapies are often expensive and require specialized laboratory facilities, limiting their accessibility in many healthcare settings.[7 -11]

Future Directions:

The future of stem cell therapy in perioperative care is closely linked to advances in regenerative medicine and biotechnology.

Emerging approaches such as stem cell-derived exosomes, gene-modified stem cells, and tissue engineering techniques may enhance therapeutic efficacy while minimizing potential risks.

Personalized regenerative medicine, in which patient-specific stem cells are used to promote healing, may become an important component of perioperative management.

Large multicenter randomized clinical trials are needed to validate the benefits of stem cell therapy and determine its role in routine surgical practice.

Conclusion:

Stem cell therapy represents a promising advancement in perioperative medicine due to its regenerative, anti-inflammatory, and immunomodulatory properties. Evidence suggests potential benefits in wound healing, surgical flap survival, orthopaedic regeneration, and organ protection following surgery. However, despite encouraging preclinical and early clinical results, significant limitations remain regarding standardization, safety, and long-term outcomes. Large-scale randomized clinical trials are required to validate the efficacy and safety of stem cell therapy in perioperative settings. With continued research and technological advances, stem cell-based therapies may become an integral component of future perioperative care.

References:

1. Casado-Díaz A. Stem Cells in Regenerative Medicine. J Clin Med. 2022;11(18):5460. Published 2022 Sep 16. doi:10.3390/jcm11185460.
2. Mahla RS. Stem Cells Applications in Regenerative Medicine and Disease Therapeutics. Int J Cell Biol. 2016;2016:6940283. doi:10.1155/2016/6940283

3. Jin Y, Li S, Yu Q, Chen T, Liu D. Application of stem cells in regeneration medicine. MedComm (2020). 2023;4(4):e291. Published 2023 Jun 17. doi:10.1002/mco2.291
4. Lee KH, Tseng WC, Yang CY, Tarng DC. The Anti-Inflammatory, Anti-Oxidative, and Anti-Apoptotic Benefits of Stem Cells in Acute Ischemic Kidney Injury. Int J Mol Sci. 2019;20(14):3529. Published 2019 Jul 19. doi:10.3390/ijms20143529
5. Bugajska-Liedtke M, Fatyga N, Brzozowski A, Bajek A, Maj M. Anaesthetics reduce the viability of adipose-derived stem cells. Adipocyte. 2024;13(1):2351870. doi:10.1080/21623945.2024.2351870
6. Thakur P, Nirmala, Kaur J, Kaushal P, Bhardwaj A, Pandit V, Stem Cells Advancement and Applications: A Regenerative Medicines, Journal of Drug Delivery and Therapeutics. 2025; 15(2):95-106 DOI: http://dx.doi.org/10.22270/jddt.v15i2.6979
7. Wei P, Jia M, Liu PM, Meng L, Li J, Yang JJ. Stem cell-based therapy and its potential in perioperative neurocognitive disorders. Br J Anaesth. 2023;131(4):e139-e142. PMID: 37587005.
8. Adelipour M, Lubman DM, Kim J. Potential applications of mesenchymal stem cells and their derived exosomes in regenerative medicine. Expert Opin Biol Ther. 2023;23(6):491-507. PMID: 37147781.
9. Essandoh K, et al. Extracellular Vesicles: A New Paradigm for Cellular Communication in Perioperative Medicine, Critical Care, and Pain Management. Anesth Analg. 2021. PMID: 34304233.
10. Tan F, Li X, Wang Z, et al. Clinical applications of stem cell-derived exosomes. Signal Transduct Target Ther. 2024;9(1):17. PMID: 38212307.
11. Abdulmalek OAHY, Husain KH, AlKhalifa HKA, et al. Therapeutic Applications of Stem Cell-Derived Exosomes. Int J Mol Sci. 2024;25(6):3562. PMID: 38542535