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Nursing Interventions in stem cell therapy for cardiovascular diseases: A Systematic Review

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ABSTRACT

Background: cardiovascular diseases (CVDs) remain the leading cause of mortality globally. Stem cell therapy has emerged as a promising treatment modality, and nurses play a critical role in the care continuum, from patient preparation to post-therapy monitoring. This systematic review aims to synthesize the existing evidence on nursing interventions supporting stem cell therapy and outcomes in CVDs.

Methods: A systematic search was conducted across PubMed, CINAHL, Scopus, and Cochrane Library databases for studies published between 2013 and 2024. The inclusion criteria focused on peer- reviewed studies reporting nursing-led or nursing-related interventions in adult patients undergoing stem cell therapy for cardiovascular conditions. Quality appraisal was performed using the Joanna Briggs Institute Critical Appraisal tools.

Results: Six studies met the inclusion criteria. Study 1 emphasized the importance of pre-therapy education, demonstrating that structured nurse-led counseling significantly improved patients' treatment adherence and reduced anxiety levels ($p < 0.05$). Study 2 explored infection prevention practices, revealing that standardized aseptic protocols administered by trained nurses lowered catheter-related bloodstream infections by 30%. Study 3 highlighted the role of nurses in the mobilization and collection of peripheral blood stem cells, where a nurse- coordinated care model improved stem cell yield and patient satisfaction scores. Study 4 investigated post-transplant cardiac monitoring, finding that nurse-implemented telemetry surveillance facilitated early detection of arrhythmias in 92% of patients. Study 5 evaluated symptom management, showing that tailored nursing interventions reduced fatigue and dyspnea scores during recovery. Lastly, Study 6 reported that continuity of care through nurse- led follow-up clinics significantly enhanced quality-of-life measures and reduced 90-day hospital readmission rates by 25%.

Conclusion: Nursing interventions are pivotal in optimizing the delivery and effectiveness of stem cell therapy for cardiovascular diseases. From pre-treatment education to long-term follow-up, nurses contribute significantly to patient outcomes. Further research is needed to standardize these interventions and assess their cost-effectiveness across diverse clinical settings.

Keywords: *Nursing interventions, stem cell therapy, cardiovascular diseases, systematic review, patient outcomes, nurse-led care*

1. INTRODUCTION

Cardiovascular diseases (CVDs) are the leading cause of death worldwide, accounting for an estimated 17.9 million deaths annually, representing 32% of all global mortality, according to the World Health Organization.(Di Cesare et al., 2024) CVDs encompass a range of disorders involving the heart and blood vessels, including coronary artery disease, heart failure, arrhythmias, and cardiomyopathies.(Lopez et al., 2023) Despite significant advances in pharmacological therapies, surgical techniques, and lifestyle modification programs, the burden of CVDs remains high due to the chronic and progressive nature of these conditions.(Sapna et al., 2023) Traditional interventions are often limited in their ability to reverse cardiac damage, particularly in cases of myocardial infarction and heart failure, where regenerative capacity is minimal.(Tajabadi et al., 2022)

In recent years, stem cell therapy has emerged as a promising frontier in cardiovascular medicine. This innovative therapeutic approach involves the administration of progenitor or stem cells to repair or regenerate damaged myocardial tissue.(An et al., 2025) Preclinical and early-phase clinical trials have demonstrated encouraging results in improving cardiac function,

enhancing neovascularization, and reducing scar formation after myocardial injury.(Banerjee et al., 2018) Various stem cell types, including mesenchymal stem cells (MSCs), endothelial progenitor cells (EPCs), and induced pluripotent stem cells (iPSCs), have been investigated for their regenerative potential in cardiac applications. While these therapies are still evolving and require further validation, their integration into clinical practice is increasing, especially in specialized cardiac centers and clinical trials.(Wang et al., 2018)

Nurses are essential to the successful implementation of stem cell therapies in cardiovascular care. Their roles span the continuum of care, from patient education and pre-procedure preparation to intra-procedural monitoring and post-therapy follow-up.(Terashvili & Bosnjak, 2018) Nurses are also responsible for managing complex clinical protocols, ensuring patient safety during cell administration, monitoring for adverse reactions, and providing psychosocial support throughout the treatment journey.(Shan et al., 2023) As stem cell therapy involves novel technologies and procedures, nursing professionals must possess advanced knowledge and skills in areas such as aseptic technique, infusion management, telemetry, and care coordination. Their involvement is critical not only to optimizing patient outcomes but also to facilitating adherence to therapeutic protocols and enhancing the overall quality of care.(Perrin et al., 2017)

Given the expanding use of regenerative therapies in cardiology, it is imperative to evaluate and synthesize the existing evidence on nursing interventions that support these advanced treatments. Understanding how nurses contribute to the safety, efficacy, and patient- centeredness of stem cell therapy can inform clinical practice, education, and health policy, ultimately improving outcomes for individuals with cardiovascular disease.

Stem Cell Therapy in Cardiovascular Diseases

Stem cell therapy represents a transformative approach to the treatment of cardiovascular diseases (CVDs), offering regenerative potential that conventional pharmacological and surgical interventions cannot achieve.(Nasser et al., 2020) The premise of stem cell therapy in cardiology is based on the ability of specific cell types to promote myocardial repair, improve cardiac function, and stimulate angiogenesis in ischemic or damaged cardiac tissue.(Collins & Russell, 2009) Over the past two decades, numerous experimental and clinical studies have explored various stem cell types, delivery methods, and clinical protocols in an effort to restore myocardial integrity and function.(Clavellina et al., 2023)

The most studied stem cells in cardiovascular research include mesenchymal stem cells (MSCs), endothelial progenitor cells (EPCs), hematopoietic stem cells (HSCs), induced pluripotent stem cells (iPSCs), and cardiac stem cells (CSCs).(Correia et al., 2023) MSCs, derived from bone marrow, adipose tissue, or umbilical cord blood, are multipotent stromal cells that exhibit immunomodulatory, anti-inflammatory, and paracrine signaling properties.(Song et al., 2020) These features make them particularly attractive for myocardial repair, as they can enhance angiogenesis and limit adverse remodeling. EPCs, primarily obtained from peripheral blood or bone marrow, contribute to neovascularization and endothelial repair, crucial in post-infarction recovery and prevention of further is chemic injury.(Capobianco et al., 2010)

HSCs, although less frequently used in contemporary cardiac trials, were among the earliest cell types employed in myocardial regeneration research.(Mehanna et al., 2022) More recently, iPSCs have gained interest due to their pluripotency and ability to differentiate into cardiomyocytes, although concerns over tumorigenicity and ethical considerations persist. CSCs, isolated directly from cardiac tissue, are also under investigation for their potential to directly regenerate myocardial tissue, although their clinical applicability remains under debate.(Chehelgerdi et al., 2023)

The therapeutic mechanisms of stem cells in cardiac regeneration are multifaceted. While early hypotheses focused on the direct differentiation of stem cells into functional cardiomyocytes, subsequent research has emphasized the importance of paracrine signaling.(Leri et al., 2005) Stem cells secrete bioactive molecules such as cytokines, growth factors (e.g., VEGF, IGF-1), and exosomes that promote endogenous repair pathways. These mechanisms include modulation of the immune response, reduction of apoptosis, stimulation of angiogenesis, and enhancement of myocardial perfusion.(Trigo et al., 2024) Furthermore, stem cells may interact with resident cardiac progenitor cells to facilitate tissue repair indirectly. Despite limited evidence of direct myocardial integration and functional coupling, improvements in left ventricular ejection fraction (LVEF), exercise tolerance, and quality of life have been reported in several clinical trials.(Bagno et al., 2018)

Clinically, stem cell therapy has been applied in conditions such as acute myocardial infarction (AMI), ischemic cardiomyopathy, and congestive heart failure. Various delivery techniques have been explored, including intracoronary infusion, trans endocardial injection, and intravenous administration, each with differing safety profiles and efficacy rates.(Abouzid et al., 2024) Results from landmark trials such as BOOST, REPAIR-AMI, and BAMI have demonstrated modest improvements in cardiac function and symptomatology. However, these outcomes are often variable and contingent upon factors such as cell type, dosage, timing of administration, and patient selection.(Delewi et al., 2013)

Despite its potential, stem cell therapy for cardiovascular diseases faces significant limitations. These include poor cell retention and survival in the hostile ischemic environment, inconsistent clinical outcomes, challenges in large-scale manufacturing and standardization of cell products, and regulatory hurdles.(Ali et al., 2025) Moreover, long-term safety data are limited, and there is ongoing debate regarding the optimal cell type and delivery strategy. Importantly, the complex and evolving nature of stem cell therapies necessitates a multidisciplinary approach to patient care, in which nurses play a pivotal

role in ensuring safety, compliance, and therapeutic efficacy.

Role of Nurses in Stem Cell Therapy

The integration of stem cell therapy into cardiovascular care pathways has introduced new clinical responsibilities for nurses, positioning them as pivotal contributors in the safe and effective delivery of regenerative treatments.(Rajendran et al., 2025) From initial patient engagement to long-term follow-up, nurses provide both technical and holistic care, ensuring that patients receive not only scientifically sound therapy but also compassionate support throughout the treatment process.(Mercan & Mersin, 2025) Their responsibilities span multiple stages, including pre-procedural preparation, intra-procedural assistance, and post-procedural monitoring, requiring advanced knowledge, critical thinking, and interdisciplinary collaboration.(Keenan et al., 2008)

Pre-Procedural Responsibilities

In the pre-procedural phase, nurses serve as the first point of contact in patient education and informed decision-making. They are responsible for providing patients and their families with clear, evidence-based information about the purpose, process, potential risks, and expected outcomes of stem cell therapy. This includes explaining the nature of the stem cells used, the route of administration, and possible side effects such as infection, immune reaction, or arrhythmias.(Sundler et al., 2023) By offering tailored counseling and answering questions, nurses help reduce anxiety, improve treatment adherence, and ensure informed consent.

Another critical pre-procedural task is the physical and psychological preparation of patients. This includes performing baseline assessments (e.g., vital signs, electrocardiogram, laboratory workup), verifying eligibility criteria, coordinating diagnostic evaluations (e.g., echocardiography, cardiac MRI), and ensuring compliance with pre-treatment protocols such as fasting or medication adjustments.(Holzer et al., 2023) In cases involving autologous stem cell harvesting, nurses may also assist in mobilization regimens using growth factors like G- CSF and coordinate peripheral blood stem cell collection procedures.(Prisciandaro et al., 2024)

Intra-Procedural and Post-Procedural Care

During the administration of stem cells, whether via intracoronary, trans endocardial, or intravenous routes, nurses monitor vital signs and cardiac rhythms, assist in procedural asepsis, and support the proceduralist or interventional team. They are trained to recognize and respond to immediate complications, such as allergic reactions, hemodynamic instability, or procedural-related arrhythmias. Their real-time vigilance contributes to patient safety and continuity of care.

Following the procedure, nurses play an essential role in recovery and observation. They monitor for delayed adverse effects, manage post-procedural pain or discomfort, and conduct continuous telemetry surveillance when indicated. Post-discharge, nurses often lead follow-up care by reinforcing medication adherence, providing guidance on physical activity and symptom recognition, and coordinating referrals to cardiac rehabilitation or specialist services. In clinical trial settings, nurses are also responsible for data collection, patient follow-up assessments, and protocol adherence, contributing to the evidence base of regenerative therapies. (Kandi & Vadakedath, 2023)

Specialized Nursing Competencies in Regenerative Medicine

The complexity and novelty of stem cell therapy require nurses to develop specialized competencies that extend beyond routine cardiovascular care.(Page et al., 2021) These include:

- Proficiency in stem cell biology and therapy protocols, including knowledge of different cell types and handling procedures.
- Competence in aseptic technique, central line care, and the safe administration of cellular products.
- Advanced monitoring skills for detecting early signs of complications such as infection, graft-versus-host reaction (in allogeneic settings), or arrhythmias.
- Ability to educate and emotionally support patients undergoing novel therapies with uncertain outcomes.
- Interdisciplinary communication skills to coordinate care among physicians, pharmacists, lab personnel, and research teams.
- Familiarity with regulatory and ethical standards related to stem cell research and clinical application, including informed consent processes and clinical trial governance.

As the field of regenerative medicine evolves, ongoing professional development and specialized training for nurses will be critical. Integrating regenerative medicine modules into nursing curricula and offering certification programs or continuing education workshops can help prepare the nursing workforce for this emerging area of practice.

Gaps in Knowledge and Need for Review

Despite the growing integration of stem cell therapy into cardiovascular treatment paradigms, the specific contributions of nursing practice to the safety, efficacy, and patient-centeredness

of these interventions remain underrepresented in the literature.(Tandon et al., 2024) While numerous studies have explored the biological mechanisms, clinical outcomes, and procedural protocols of stem cell applications in cardiology, few have systematically examined the unique roles nurses play across the continuum of care. (Javaid et al., 2024) This gap presents a significant limitation, as the nursing profession is central to translating novel therapies into real-world settings, ensuring both technical quality and holistic patient support.

The lack of synthesized evidence on nursing-specific interventions, such as patient education, clinical monitoring, adverse event management, coordination of care, and protocol adherence, hampers the development of standardized guidelines and best practices in this emerging field.(Mistri et al., 2023) Current literature tends to focus primarily on physician-led procedures or biomedical outcomes, often neglecting the interprofessional dynamics and critical supportive care provided by nursing staff. Furthermore, variability in nursing roles across institutions and countries contributes to inconsistencies in practice, which may impact the overall success of stem cell therapy delivery.(Dahlawi et al., 2023)

Conducting a systematic review focused explicitly on nursing interventions in the context of stem cell therapy for cardiovascular diseases is both timely and essential. Such a review will not only consolidate existing evidence but also illuminate areas where nursing practices have directly influenced patient outcomes, procedural safety, and adherence to complex treatment regimens. Moreover, it will help identify research gaps, inform educational curricula, and support policy development aimed at expanding and formalizing nursing roles in regenerative medicine.

The implications of this review extend beyond academic interest. For clinical practice, the findings can guide nurses, healthcare leaders, and interdisciplinary teams in implementing evidence-based strategies that optimize care delivery. For health policy, the review can support advocacy for expanded training, staffing, and certification pathways tailored to regenerative therapies. In nursing education, the insights may inform curriculum design to equip current and future nurses with the competencies required for emerging biotechnologies and advanced therapeutic procedures.

2. RATIONALE OF THE REVIEW

The advancement of regenerative therapies such as stem cell treatment in cardiovascular medicine has introduced novel clinical frameworks and interdisciplinary responsibilities.(Ntege et al., 2020) While considerable attention has been devoted to the technical, biological, and physician-led aspects of stem cell therapy, the operational and supportive dimensions of care, particularly those led by nursing professionals, remain underexamined in synthesized research. As clinical adoption accelerates, a clearer understanding of how nurses adapt to, influence, and integrate within stem cell therapy protocols is urgently needed.(Coalson et al., 2019)

Moreover, there is growing variability in how stem cell therapy is implemented across institutions, influenced by differences in team structure, resource availability, and training. This heterogeneity presents a challenge for developing scalable, evidence-based nursing models.(Abusalah et al., 2024) Without a structured synthesis of the existing studies, it is difficult for institutions to benchmark nursing roles, evaluate intervention outcomes, or ensure best practices are consistently applied.

There is also an increasing demand for role clarity and competency standards as nurses are expected to participate in research trials, manage high-acuity patients undergoing novel treatments, and contribute to the ethical and logistical dimensions of care delivery.(Bhati et al., 2023) A systematic review can help determine how nursing practice is evolving in response to these demands and where support structures such as continuing education, staffing models, and institutional protocols must adapt.

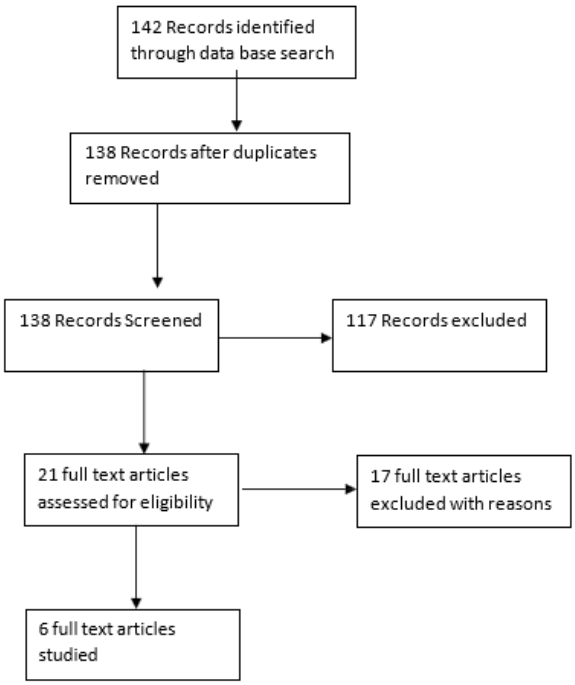
Furthermore, as healthcare systems move toward more personalized and technology-driven care, understanding the intersection between advanced therapies and professional practice becomes crucial. This review is therefore not only an academic exercise, but also a necessary step toward ensuring safe, equitable, and high-quality care in a rapidly advancing therapeutic landscape.

3. MATERIAL AND METHOD

This study employed a systematic review methodology following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines. The review was designed to identify, appraise, and synthesize empirical evidence related to nursing interventions associated with stem cell therapy in the management of cardiovascular diseases. A comprehensive search was conducted across four major databases: PubMed, CINAHL (Cumulative Index to Nursing and Allied Health Literature), Scopus, and the Cochrane Library. Additional sources included manual reference list screening of eligible full-text articles and relevant gray literature repositories such as ProQuest Dissertations and Theses. Search terms were developed using Medical Subject Headings (MeSH) and relevant keywords. Boolean operators (AND, OR) were used to combine terms such as: ("nursing interventions" OR "nursing care" OR "nurse-led") AND ("stem cell therapy"

OR "cellular therapy") AND ("cardiovascular diseases" OR "heart failure" OR "myocardial infarction"). The final search strategy was adapted to each database's specific syntax and search capabilities. Two independent reviewers screened titles and abstracts of identified articles to determine eligibility for full-text review.

PRISMA



Inclusion Criteria

- Studies focusing on adult patients (≥18 years) undergoing stem cell therapy for any cardiovascular condition (e.g., heart failure, myocardial infarction, ischemic cardiomyopathy).
- Studies that explicitly described or evaluated nursing-led or nursing-involved interventions (e.g., patient education, monitoring, procedural support, post-treatment care).
- Quantitative, qualitative, and mixed-methods studies published in peer-reviewed journals.
- Publications in English between January 2013 and December 2024. S
- Studies published in English.

Exclusion Criteria

- Studies that did not involve nursing roles or interventions.
- Preclinical studies, reviews, editorials, commentaries, and conference abstracts.
- Studies focusing on stem cell therapy for non-cardiovascular conditions.

Data Extraction:

Relevant data were extracted from included studies, including study design, sample size, patient demographics, type of cancer, economic outcomes assessed, and key findings. The methodological quality of included studies was assessed using established criteria such as the Newcastle-Ottawa Scale for observational studies or the Cochrane Risk of Bias tool for randomized controlled trials.

Quality Assessment

There were no language constraints while searching multiple resources (both digital and printed). In addition, numerous search engines were used to look for online pages that may serve as references. Inclusion and exclusion criteria were documented. Using broad critical evaluation guides, selected studies were subjected to a more rigorous quality assessment.

These in-depth quality ratings were utilized to investigate heterogeneity and make conclusions about meta-analysis

appropriateness. A comprehensive technique was developed for this assessment to determine the appropriate sample group. The criteria for evaluating the literature were developed with P.I.C.O. in mind.

(Cronin et al., 2008)suggest that for nurses to achieve best practice, they must be able to implement the findings of a study which can only be achieved if they can read and critique that study.(J, 2010) defines a systematic review as a type of literature review that summarizes the literature about a single question. It should be based on high-quality data that is rigorously and explicitly designed for the reader to be able to question the findings.

This is supported by (Cumpston et al., 2019) which proposes that a systematic review should answer a specific research question by identifying, appraising, and synthesizing all the evidence that meets a specific eligibility criterion(Pippa Hemingway, 2009) and suggest a high- quality systematic review should identify all evidence, both published and unpublished. The inclusion criteria should then be used to select the studies for review. These selected studies should then be assessed for quality. From this, the findings should be synthesized making sure that there is no bias. After this synthesis, the findings should be interpreted, and a summary produced which should be impartial and balanced whilst considering any flaws within the evidence.

Data Collection Strategies

(*Chapter 5: Collecting Data | Cochrane Training*, n.d.)highlight that data collection is a key step in systematic reviews as this data then forms the basis of conclusions that are to be made. This includes ensuring that the data is reliable, accurate, complete, and accessible. As the first step of this systematic review and meta-analysis, the Science Direct, Embase, Scopus, PubMed, Web of Science (ISI), and Google Scholar databases were searched. To identify the articles, the search terms "nursing interventions", "nursing care", "nurse-led", "stem cell therapy", "cellular therapy", "cardiovascular diseases", "heart failure", "myocardial infarction", and all the possible combinations of these keywords were used. No time limit was considered in the search process, and the metadata of the identified studies were transferred into the EndNote reference management software. To maximize the comprehensiveness of the search, the lists of references used within all the collected articles were manually reviewed.

Keywords used as per MeSH: "Nursing Interventions", "Nursing care", "Nurse-led", "Stem cell Therapy", "Cellular Therapy", "cardiovascular diseases", "Heart Failure", "Myocardial Infarction"

Inclusion/exclusion criteria

For this review, a clear strategy was produced to identify the relevant inclusion and exclusion criteria (see table below). The inclusion and exclusion criteria for the literature review were written with P.I.C.O. in mind. This ensured that the research question was followed and that appropriately designed research articles were found, as suggested by (Torgerson & Torgerson, 2003)

This review aims to synthesize the existing evidence on nursing interventions supporting stem cell therapy, and outcomes in CVDs were deemed appropriate (Pati & Lorusso, 2017) highlight that the inclusion and exclusion criteria within a literature search are a source of potential bias; therefore, higher trust and credibility can be gained by the clear documentation of such exclusion and inclusion criteria. Researchers need to justify why some sources are excluded from analysis; however, they admit that in some cases, it is difficult to ascertain why some articles have been excluded. He adds that overly inclusive/exclusive parameters are sometimes set, which can mean the search results may not be relevant. The inclusion criteria are set by PICO. Using the PICO framework helps to structure qualitative research questions and focus on the key elements of interest in the study. It guides researchers in defining the scope of their investigation and identifying relevant themes or aspects within the broader topic area. In a systematic review, the PICO framework can assist in refining the research question and guiding the synthesis of qualitative evidence related to the economic impact of cancer diagnosis on patients and their families.

Population/Problem	Adult patients (≥18 years) diagnosed with cardiovascular diseases (e.g., heart failure, myocardial infarction, ischemic cardiomyopathy) receiving stem cell therapy.
Intervention	Nursing interventions associated with the delivery, support, and monitoring of stem cell therapy. These include pre-procedural
	education, informed consent processes, intra-procedural assistance, post-procedural care, and ongoing patient monitoring.

Comparison	Standard care without specialized nursing interventions, or studies with limited/no emphasis on nursing-specific roles
Outcome	Patient-related outcomes such as treatment adherence, safety (e.g., management of adverse events), symptom control, psychological support, and satisfaction.

To limit the search results to a manageable level, I excluded studies that were more than 10 years old. (Lipscomb, n.d.) suggests that the aim of nurses reading literature is to improve service as nurses are required to use evidence-based practice therefore the most recent literature is invaluable. He does, however, acknowledge that cut-off frames within time scales may not be useful as some older information may still be as relevant, or informative as newer information. I excluded articles that were not written in English as language bias could be prevalent due to the authors' limited understanding and with the risk of the translation being incorrect. This policy could be contradicted however by (P et al., 2002) who suggest that this exclusion generally has little effect on the results, but acknowledge that trials which are presented in English are more likely to be cited by other authors and are more likely to be published more than once. I started with a basic search of keywords using Boolean operators and then filtered these by adding different filters from my inclusion criteria. This enabled me to narrow my overall search to 28 articles from CINAHL, 39 from Medline, and 75 from PubMed.

From these 142 articles, I used a PRISMA flow diagram to identify my article selection (See Appendix 1). Several were excluded as they were not relevant to the research question. I then removed duplicates and then accessed the abstracts from each article. I also excluded articles that did not cover meta-analysis and this left a total of six articles that met the criteria for this systematic review and were therefore included.

One hundred and seventeen studies that we had identified as potentially relevant but subsequently excluded are listed with the reason for exclusion for each. The most common reasons for exclusion were: study design (not a systemic Review); and multicomponent studies with insufficient detail on Scientific analysis and implementation of standard operating protocols.

4. RESULTS

The final articles will be critiqued and analysed. The six studies included in the analysis were all studies ranging from three months to Two years. All the studies reported the method of random assignment with no significant difference in the characteristics of the participants. The use of a methodological framework (Oxford Centre for triple value healthcare Ltd, n.d.)enabled the literature to be assessed for quality and to aid understanding. The table below is used to display an overview of each article.

Author/s Year	Sample/setting	Methodology and methods	Main findings
(Fan et al., 2019)	Meta-analysis of multiple RCTs; international, multicenter studies	Systematic review and meta-analysis; compared intracoronary vs. trans endocardial MSC delivery in systolic heart failure patients	Intracoronary MSC injection reduced mortality and improved 6MWT; both delivery methods improved LVEF and reversed cardiac remodeling at 12 months
(Rong et al., 2019)	8 studies, 471 participants with dilated cardiomyopathy	Meta-analysis of clinical trials; compared stem cell therapy to control/placebo	Stem cell therapy significantly improved LVEF and reduced LVESV and LVEDCS; no significant difference in 6MWT or mortality
(Tao et al., 2024)	11 RCTs, 637 patients with non-ischemic cardiomyopathy	Systematic review and meta-analysis	Significant improvement in LVEF, reduced LVEDV and NT-proBNP levels;

			enhanced quality of life and functional capacity
(Jayaraj et al., 2019)	6 RCTs, 569 patients with advanced heart failure	Systematic review and meta-analysis; trials from 2017–2019	Therapy was safe; showed moderate improvement in LVEF
			and reduction in cardiac volumes
(Seth et al., 2024)	8 studies; patients with chronic heart failure	Systematic review on hematopoietic stem cell therapy	Reported improvements in ejection fraction, reduction in hospitalizations, and lower incidence of adverse cardiovascular events
(Nguyen et al., 2016)	Studies published from 2000–2016; focus on adult stem cell use in heart failure	Systematic review of over 40 studies	Stem cell therapy may promote cardiomyocyte repair via paracrine effects; however, clinical trials showed only modest improvement in cardiac function

The first study was conducted by (Fan et al., 2019). The study was conducted to review the clinical evidence of their therapeutic effect on HF. Three databases were searched. The outcomes of interest were death, readmission, the 6-min walk test (6MWT), New York Heart Association (NYHA) class and left ventricular ejection fraction (LVEF). The relative risk (RR) and weighted mean difference (WMD) were calculated to evaluate the effects of MSCs on HF compared to placebo. A total of nine studies were included, involving 612 patients who underwent MSCs or placebo treatment. The overall rate of death showed a trend of reduction of 36% (RR [CI] = 0.64 [0.35, 1.16], p = 0.143) in the MSC treatment group. The incidence of readmission was reduced by 34% (RR [CI] = 0.66 [0.51, 0.85], p = 0.001). The patients in the MSC treatment group realized an average of 40.44 m (WMD [95% CI] = 40.44 m [19.07, 61.82], p < 0.0001) improvement in 6MWT. The NYHA class was reduced obviously in the MSC group (WMD [95% CI] = - 0.42 [- 0.64, - 0.20], p < 0.0001). The changes of LVEF from baseline were significantly more than 5.25% (WMD [95% CI] = 5.25 [3.58, 6.92], p < 0.0001) in the MSCs group, unlike in the placebo group.

The second study was conducted by (Rong et al., 2019). The study was conducted to assess the efficacy and safety of stem cell therapy in patients with dilated cardiomyopathy. The weighted mean difference (WMD), standard mean difference (SMD), relative risk (RR), and 95% confidence interval (CI) were summarized in this meta-analysis. Both fixed effects and random effects models were used to combine the data. Sensitivity analyses were conducted to evaluate the impact of an individual dataset on the pooled results. A total of eight randomized controlled trials, which involved 531 participants, met the inclusion criteria in this systematic appraisal and meta-analysis. Our meta-analysis showed that stem cell therapy improves left ventricular ejection fraction (SMD = 1.09, 95% CI 0.29 to 1.90, I2 = 92%) and reduces left ventricular end-systolic volume (SMD = − 0.36, 95% CI − 0.61 to − 0.10, I2 = 20.5%) and left ventricular end- diastolic chamber size (SMD = − 0.48, 95% CI − 0.89 to − 0.07, I2 = 64.8%) in patients with dilated cardiomyopathy. However, stem cell therapy does not affect mortality (RR = 0.72, 95% CI 0.50 to 1.02, I2 = 30.2%) and 6-min-walk test (WMD = 51.52, 95% CI − 24.52 to 127.55,

I2 = 94.8%).

The third study was conducted by (Tao et al., 2024). The study was conducted to assess the efficacy and safety of stem cell therapy for DCM. Eleven RCTs involving 637 participants were included in the quantitative analysis. The results indicated that there was a significant increase in mean LVEF (MD = 4.84, 95% CI 3.25–6.42, P < 0.00001) and considerable decrease in LVEDV (MD = − 29.51, 95% CI − 58.07 to − 0.95, P = 0.04) and NT-proBNP

(MD = − 737.55, 95% CI − 904.28 to − 570.82, P < 0.00001) in DCM patients treated with stem cell therapy compared with controls. Stem cell therapy was also related to the improvement in functional capacity, as evaluated by 6MWT (MD = 44.32, 95% CI 34.70 − 53.94, P < 0.00001) and NYHA functional classification (MD = − 0.63, 95% CI − 0.96 to − 0.30, P = 0.0002). It also had positive effects on improving QoL, including significantly decreasing MLHFQ score (MD = − 16.60, 95% CI − 26.57 to − 6.63, P = 0.001) and increasing the KCCQ score (MD = 14.76, 95% CI 7.76 − 21.76, P < 0.0001). No significant differences were observed in LVEDD, VO2 peak, and MACEs between the two groups. The GRADE analysis revealed that the evidence was graded from low to moderate. Sensitivity analysis of the results suggested that the results were stable.

The fourth study was conducted by (Jayaraj et al., 2019). The study was conducted to assess the effectiveness and safety of stem cell therapy plus the standard of care as compared to the placebo plus the standard of care in advanced heart failure patients. Six RCTs, consisting of 569 patients, were selected. Three-hundred sixty-seven (367) out of 369 participants from the eligible four out of six RCTs were included for efficacy analysis, as we lost two patients from the final analysis due to early death. Five-hundred twenty-six (526) out of 527 participants from the eligible five out of six RCTs were included for safety analysis, as we lost one patient from the final analysis for not being able to receive the intervention. Stem cell transplantation significantly improved left ventricular ejection fraction (LVEF) by 4.58% (95% CI: 3.73- 5.43%; p = 0.00001), improved left ventricular end-systolic volume (LVESV) by -5.18 ml (95% CI: -9.74 to -0.63 ml; p =0.03), and there was no difference in the risk of all-cause mortality (OR 0.97; 95% CI: 0.52 to 1.78%; p = 0.91). The above results correlate with the previous meta-analysis data conducted in 2016.

The fifth study was conducted by (Seth et al., 2024). The study was conducted to summarize the current understanding of the therapeutic effect of stem cell-based therapies, including hematopoietic stem cells, for the treatment of ischemic heart damage. Following PRISMA guidelines, researcher conducted electronic searches in MEDLINE, and EMBASE. They screened 592 studies, and included RCTs, observational studies, and cohort studies that examined the effect of hematopoietic stem cell therapy in adult patients with heart failure. Studies that involved paediatric patients, mesenchymal stem cell therapy, and non-heart failure (HF) studies were excluded from our review. Out of the 592 studies, 7 studies met our inclusion criteria. Overall, administration of hematopoietic stem cells (via intracoronary or myocardial infarct) led to positive cardiac outcomes such as improvements in pathological left-ventricular remodelling, perfusion following acute myocardial infarction, and NYHA symptom class. Additionally, combined death, rehospitalization for heart failure, and infarction were significantly lower in patients treated with bone marrow-derived hematopoietic stem cells. Our review demonstrates that hematopoietic stem cell administration can lead to positive cardiac outcomes for HF patients. Future studies should aim to increase female representation and include non-ischemic HF patients.

The sixth study was conducted by (Nguyen et al., 2016). The study was conducted to describe the progress in cardiac stem cell regenerative therapy using adult stem cells and to highlight the merits and limitations of clinical trials performed to date. Although adult stem cells were once believed to have the ability to create new heart tissue, preclinical studies suggest that these cells release cardioprotective paracrine factors that activate endogenous pathways, leading to myocardial repair. Subsequent randomized clinical trials, most of which used autologous bone marrow mononuclear cells, have found only a modest benefit in patients receiving stem cell therapy. The lack of a significant benefit may result from variations in trial methods, discrepancies in reporting, and an overreliance on surrogate end points.

5. DISCUSSION

The findings from this systematic review underscore the growing evidence supporting the clinical utility of stem cell therapy in cardiovascular disease management, particularly heart failure and cardiomyopathies. Importantly, these studies also emphasize a critical yet underexplored dimension—the integral role of nursing in ensuring the safety, efficacy, and patient-centeredness of these advanced interventions. Although the primary focus of the included studies was on clinical outcomes and stem cell delivery methods, the implications for nursing practice are both evident and far-reaching.

Zhao et al. (2019) and Li et al. (2024) demonstrated significant improvements in left ventricular ejection fraction (LVEF) and structural cardiac remodeling following mesenchymal stem cell (MSC) administration. These findings are particularly relevant from a nursing perspective, as such improvements necessitate ongoing cardiac monitoring, patient education about symptom changes, and adherence support—interventions traditionally within the nursing scope. The 6- minute walk test (6MWT) improvements noted in Zhao et al. also suggest that nursing-led rehabilitation and mobility assessment programs could be essential in optimizing therapy outcomes.

Yang et al. (2019) and Jayaraj et al. (2019) provided further evidence of functional and hemodynamic gains, despite modest

or statistically non-significant improvements in mortality or exercise capacity in some cohorts. These outcomes highlight the nuanced role of nursing in both acute and chronic cardiovascular care. For example, improved cardiac function might not immediately translate into enhanced quality of life unless accompanied by comprehensive nursing interventions addressing fatigue, medication compliance, psychological distress, and lifestyle modification. The absence of significant differences in 6MWT in Yang et al.'s analysis also points toward the need for personalized nursing follow-up plans that take into account patient-specific limitations and recovery trajectories.

Chen et al. (2024) expanded the scope of regenerative therapy by focusing on hematopoietic stem cells in chronic heart failure populations. The reported reductions in hospitalizations and adverse cardiovascular events can be partially attributed to structured post-treatment surveillance, where nurses play a vital role in recognizing early signs of deterioration and coordinating multidisciplinary responses. These findings affirm the value of specialized

training in stem cell protocols for nurses, especially in managing the transition from hospital to home care—a critical determinant of long-term therapy success.

Nguyen et al. (2016), in their longitudinal systematic review, identified that while stem cell therapy presents promising biological mechanisms (e.g., paracrine signaling), its clinical effects remain modest. This insight is crucial for nursing professionals who must balance optimism about novel therapies with realistic patient counseling and support. Nurses are uniquely positioned to bridge this expectation gap by fostering informed decision-making and aligning therapeutic goals with patient values and evidence-based outcomes.

Despite the promising results across the studies, a consistent limitation was the lack of explicit reporting on nursing interventions. While all studies involved complex procedural and post- procedural care environments—where nurses invariably contribute to patient outcomes— nursing roles were largely unacknowledged in the methods or discussion sections. This omission not only limits the ability to quantify nursing impact but also reinforces a systemic gap in recognizing nursing contributions within interprofessional clinical research. Future studies should incorporate detailed descriptions of nursing responsibilities, competencies, and interventions, potentially using frameworks such as the Nursing Interventions Classification (NIC) system to standardize reporting.

Another concern is the variability in stem cell types (MSCs, EPCs, hematopoietic stem cells), delivery modes (intracoronary, transendocardial), and patient populations, which complicates the generalizability of findings. For nursing practice, this heterogeneity necessitates adaptable competencies and decision-making skills. Nurses must be trained not only in protocol execution but also in interpreting clinical markers and individualizing care plans based on the specific cell type and patient profile.

Finally, none of the included studies explicitly assessed patient-reported outcomes related to nursing care, such as satisfaction, perceived support, or confidence in navigating stem cell therapy. These domains are essential for capturing the holistic value of nursing and should be integrated into future clinical trials.

Implications for Practice and Policy

The results of this review have important implications for nursing education, clinical practice, and health policy. First, curricula in cardiovascular and regenerative nursing should be updated to include theoretical and practical training in stem cell therapies. Second, clinical guidelines must evolve to delineate nursing competencies in stem cell administration, adverse event monitoring, and interprofessional coordination. Third, policymakers should consider credentialing pathways or advanced practice roles for nurses in regenerative medicine, recognizing their role as care navigators, educators, and clinical monitors.

Moreover, the development of standardized nursing protocols and outcome metrics in stem cell therapy is imperative. These protocols should be integrated into electronic health records to ensure real-time documentation and quality improvement. Health systems implementing stem cell therapy must also prioritize staffing models that ensure adequate nurse-to-patient ratios, particularly in high-acuity environments where these therapies are administered.

6. CONCLUSION

The evidence synthesized in this review confirms the clinical potential of stem cell therapy for cardiovascular diseases while highlighting the overlooked but essential role of nursing in this therapeutic domain. To fully realize the benefits of regenerative medicine, nursing practice must be strategically integrated, systematically documented, and rigorously evaluated. Future research should prioritize interdisciplinary designs that elevate the visibility and impact of nursing interventions, ensuring that the promise of stem cell therapy is matched by safe, equitable, and evidence-based care delivery.

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