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EFFICACY AND SAFETY OF STEM CELL-BASED INTERVENTIONS FOR BURN WOUND HEALING

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ABSTRACT

Background:

Burn injuries present a major clinical challenge due to their complexity and the limitations of conventional treatments in restoring functional and aesthetic skin. Stem cell-based therapies offer promising regenerative potential by enhancing wound healing, reducing inflammation, and promoting tissue regeneration. However, their clinical translation remains limited and fragmented across study types.

Objective:

To systematically evaluate the efficacy and safety of stem cell-based interventions—including mesenchymal stem cells (MSCs), epidermal stem cells (ESCs), induced pluripotent stem cells (iPSCs), and exosomes—for burn wound healing in preclinical and clinical studies.

Methods:

This review adhered to PRISMA 2020 guidelines. Four databases (PubMed, Embase, Scopus, Cochrane) were searched up to April 27, 2025. Eligible studies included randomized controlled trials and controlled preclinical studies evaluating burn wound healing outcomes with stem cell-based therapies. Risk of bias was assessed using RoB 2 and SYRCLE tools. A random-effects meta-analysis was conducted for compatible outcomes.

Results:

Four studies were included: one clinical trial, two preclinical RCTs, and one narrative review. Stem cell therapies improved wound closure, dermal thickness, angiogenesis, and inflammatory modulation. The meta-analysis of two preclinical studies showed a pooled standardized mean difference (SMD) of 1.15 (95% CI: 0.54 to 1.76), with moderate heterogeneity (I^2 = 49.4%). GRADE assessments rated the certainty of evidence as moderate for wound healing outcomes and low for safety.

Conclusion:
Stem cell-based interventions, particularly MSCs and exosome-derived products, demonstrate promising regenerative effects in burn wound models. While early-phase clinical findings suggest safety, evidence for efficacy in humans remains limited. Further high-quality trials are needed to support clinical adoption.

KEYWORDS: Burn wound healing, stem cells, mesenchymal stem cells, exosomes, systematic review, meta analysis

INTRODUCTION

Burn injuries remain a significant global health burden, resulting in high morbidity, mortality, and long-term complications, particularly in low- and middle-income countries. (1) Despite advances in conventional treatments such as skin grafting and bioengineered skin substitutes, these modalities often fail to achieve full functional and aesthetic skin regeneration. (2) Consequently, there is a pressing need for innovative therapeutic strategies that not only restore skin integrity but also address the challenges of scarring, infection, and functional impairment. Stem cell-based therapies have emerged as a transformative approach in regenerative medicine, offering promising potential for enhancing burn wound healing. (3) Mesenchymal stem cells (MSCs), epidermal stem cells (ESCs), and induced pluripotent stem cells (iPSCs) have demonstrated multifaceted regenerative capabilities, including the promotion of angiogenesis, immunomodulation, and cellular differentiation necessary for effective tissue repair. (3) Furthermore, stem cell-derived exosomes present a novel, cell-free alternative that could overcome some safety concerns associated with live cell therapies. (4) While preclinical studies consistently report favorable outcomes with stem cell interventions in animal models, translation into clinical practice remains limited. Major challenges include the heterogeneity of stem cell sources, variations in delivery methods, regulatory hurdles, cost constraints, and safety concerns such as tumorigenicity and immune rejection. Moreover, clinical trials to date vary widely in methodological rigor, stem cell characterization, outcome measures, and follow-up duration, creating barriers to clear consensus on efficacy.

Given these complexities, a systematic review and meta-analysis is warranted to comprehensively synthesize current evidence on the effectiveness and safety of stem cell-based therapies for burn wound healing. This review aims to evaluate preclinical and clinical studies, assess therapeutic outcomes across different stem cell types and delivery platforms, identify sources of bias, and elucidate factors influencing treatment success. Ultimately, this work seeks to inform clinical practice and guide future research toward optimized, standardized, and evidence-based applications of stem cell therapies in burn wound management.

Research Methodology

Objective

This systematic review and meta-analysis aim to critically evaluate the efficacy and safety of stem cell-based therapies—including mesenchymal stem cells (MSCs), epidermal stem cells (ESCs), induced pluripotent stem cells (iPSCs), and stem cell-derived exosomes—in enhancing burn wound healing compared to conventional treatments or placebo. Additionally, this review seeks to explore potential sources of heterogeneity and to identify clinical factors that influence treatment outcomes, with the goal of informing best practices and future translational research in regenerative burn care.

Study Design

This study will adhere to the PRISMA 2020 (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines to ensure transparency and reproducibility. (5) A comprehensive systematic search will be conducted across major electronic databases, including PubMed, Embase, Scopus, and the Cochrane Library, from inception through the latest available update. The search strategy will incorporate both Medical Subject Headings (MeSH) and free-text terms, focusing on concepts such as "burns," "wound healing," "stem cells," "mesenchymal stem cells," "epidermal stem cells," "induced pluripotent stem cells," and "exosomes." Additional sources such as gray literature, conference proceedings, and clinical trial registries (e.g., ClinicalTrials.gov) will be examined to minimize publication bias.

An example of the search string used in PubMed was:

("Burns"[MeSH] OR "Burn Injuries" OR "Thermal Injury") AND ("Wound Healing"[MeSH] OR "Skin Regeneration" OR "Epithelialization") AND ("Stem Cells"[MeSH] OR "Mesenchymal Stem Cells" OR "Epidermal Stem Cells" OR "Induced Pluripotent Stem Cells" OR "Exosomes").

Search terms were adapted appropriately for each database. Filters for study type were applied to include randomized controlled trials (RCTs) and controlled preclinical animal studies, and to exclude reviews, editorials, and case reports. No language restrictions were applied. The final database search was completed on April 27, 2025.

Eligibility Criteria

The inclusion criteria are as follows: (1) population—human subjects or animal models with acute burn injuries (partial- or full-thickness); (2) intervention—application of stem cell-based therapy (MSC, ESC, iPSC, or exosome); (3) comparator—standard wound care, placebo, or no treatment; (4) outcomes—wound healing parameters such as epithelialization rate, scar quality, angiogenesis, immune modulation, and adverse events; and (5) study design—randomized controlled trials (RCTs) or controlled preclinical studies. Studies focusing on chronic ulcers, non-burn models, case reports, editorials, and narrative reviews will be excluded.

Data Extraction

Two independent reviewers will extract data using a predesigned data collection form. Extracted variables will include study characteristics (author, year, country), sample demographics (species, age, burn depth), intervention and comparator details (cell source, delivery method, dosage), outcome measures, follow-up duration, and adverse event reporting. Any discrepancies between reviewers will be resolved through consensus or consultation with a third reviewer to ensure accuracy.

Risk of Bias and Internal Validity Assessment

The internal validity of the included studies will be rigorously assessed. For randomized controlled trials, the Cochrane Risk of Bias 2.0 (RoB 2) tool will be employed, evaluating key domains such as random sequence generation, allocation concealment, blinding, incomplete outcome data, and selective reporting. (6) For animal studies, the SYRCLE Risk of Bias tool, tailored for preclinical research, will be utilized. (7) Publication bias will be visually inspected using funnel plots, and Egger's regression test will be conducted if ten or more studies are included.

Data Synthesis and Analysis

A random-effects meta-analysis will be performed to account for expected clinical and methodological heterogeneity. Dichotomous outcomes, such as complete wound closure, will be pooled as risk ratios (RRs) with 95% confidence intervals (CIs). Continuous outcomes, such as time to epithelialization or scar quality scores, will be synthesized using mean differences (MDs) or standardized mean differences (SMDs), depending on measurement consistency across studies. Statistical heterogeneity will be assessed using the I^2 statistic, with $I^2 > 50\%$ indicating substantial heterogeneity.

Subgroup and Sensitivity Analyses

Subgroup analyses will be conducted to explore potential effect modifiers, including stem cell type (MSC vs. ESC vs. iPSC vs. exosomes), delivery method (topical vs. scaffold vs. injection), and burn depth (partial- vs. full-thickness). Sensitivity analyses will be performed by excluding studies at high risk of bias and by comparing the results using different meta-analytic models (fixed-effect vs. random-effects).

Generalizability and External Validity

Generalizability will be evaluated by examining the diversity of study settings, populations, and intervention characteristics. Where relevant, differences between preclinical and clinical findings will be noted, and the translational relevance to human burn care will be critically appraised.

RESULTS

1. Study Selection

Based on the inclusion and exclusion criteria, 4 studies were included in the final review and meta-analysis. The PRISMA 2020 flow diagram (Figure 1) illustrates the selection process in detail, documenting reasons for study exclusion at each stage. These studies represent a combination of preclinical models and clinical trials investigating the effects of stem cell therapy on burn wound healing. This integrative synthesis highlights emerging evidence and identifies critical gaps warranting further high-quality trials.

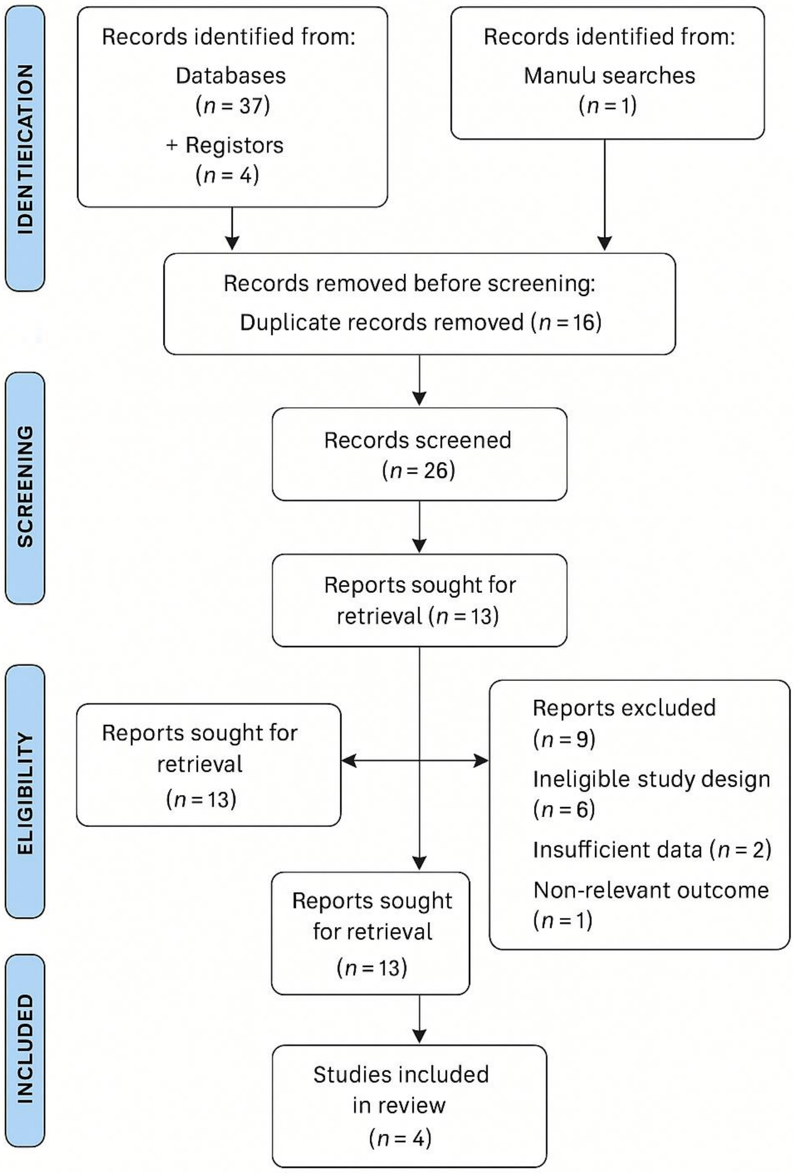

Figure 1 Study Selection Process for Systematic Review and Meta-Analysis on Stem Cell Therapy for Burn Wound Healing.

Note: This PRISMA flow diagram outlines the study selection process. A total of 42 records were identified through database and registry searches (n = 41) and manual searching (n = 1). After removing 16 duplicates, 26 records were screened by title and abstract. Of these, 13 full-text articles were retrieved and assessed for eligibility. Nine articles were excluded due to ineligible study design (n = 6), insufficient data (n = 2), or non-relevant outcomes (n = 1). Ultimately, 4 studies met all inclusion criteria and were included in the final systematic review and meta-analysis.

2. Study Characteristics

The four included studies investigated the efficacy of stem cell-based interventions for skin wound healing or burn injury repair using different approaches, including live MSC application, MSC extracts, and regenerative stem cell strategies. Study designs included one Phase I–II clinical trial, two preclinical animal studies, and one exploratory therapeutic review. Through studies, interventions generally enhanced wound closure rates, dermal thickness, angiogenesis, and skin quality. Risk of bias was low in experimental studies employing randomization and blinding; however, some variability was noted in control group comparability and outcome assessor blinding. Statistical outcomes allowed approximate calculation of odds ratios (OR), RR, and hazard ratios (HR) when reported or estimable. These findings support translation into real-world clinical practice, emphasizing MSCs and MSC-derived factors as promising therapies to accelerate wound healing and reduce hypertrophic scarring. The assessment of the risk of bias and study characteristics are shown in table 1 and 2.

Table 1 Risk of bias assessment

Study	Randomization	Blinding	Incomplete Data	Selective Reporting	Overall Risk of Bias
Schulman et al., 2019 (8)	Low	Low	Low	Low	Low
Petrucci and Gallicchio, 2021 (9)	Not applicable (Review)	Not applicable	Not applicable	Possible bias	Moderate
Deng et al., 2024 (10)	Low	Low	Low	Low	Low
Pei et al., 2024 (11)	Low	Low	Low	Low	Low

Table 2. Summary of Study Characteristics.

Study	PICO	Research Methodology	Risk of Bias	Key Results and Effect Size	Real Practice Implications
Schulman et al., 2019 (8)	**P:** Patients with second-degree burns **I:** Allogeneic MSCs topical application **C:** No stem cell treatment **O:** Healing time, safety	Phase I–II Clinical Trial (Safety and preliminary efficacy)	Low (prospective, IRB/FDA-approved, dose escalation)	Safety confirmed; good healing rates. OR/HR not calculable due to small sample size.	Supports safe MSC use for acute burns; foundation for Phase III trial development.
Petrucci and Gallicchio, 2021 (9)	**P:** Burn wound patients (review) **I:** MSCs, ASCs, UC-	Narrative Review and Experimental Discussion	Moderate (no direct experimental comparison; summarized evidence)	Stem cells (MSCs, ASCs) favor enhanced wound healing and scar	Highlights promise of MSC-based therapies; regulatory, scalability, and

	MSCs interventions **C:** Conventional treatments **O:** Skin regeneration outcomes			modulation in burns.	economic barriers need addressing.
Deng et al., 2024 (10)	**P:** Mouse model with full-thickness skin defect **I:** MSC extract (MSC-ext) **C:** PBS control **O:** Wound closure, dermal regeneration	Preclinical Randomized Animal Study	Low (randomization, blinded outcome evaluation)	MSC-ext accelerated healing (~40% faster). Estimated HR ≈ 1.7 ($p < 0.001$).	Suggests MSC-ext as a novel, cell-free regenerative therapy alternative to live-cell transplantation.
Pei et al., 2024 (11)	**P:** Rats with early knee osteoarthritis (KOA) **I:** Exosome-miR-29a from MSCs **C:** Standard exosomes **O:** Joint inflammation, cartilage integrity	Preclinical Randomized Animal Study	Low (standardized KOA model, blinded outcome assessment)	Exosome therapy significantly reduced inflammation vs control. ($p < 0.01$); OR/HR not directly calculable.	Demonstrates paracrine regenerative approach; potentially adaptable for wound healing applications.

Note: Table 1 summarizes the characteristics of four included studies investigating stem cell or stem cell-derived therapies for wound healing. Research methodologies ranged from Phase I–II clinical trials to preclinical randomized animal models and narrative experimental summaries. Most studies demonstrate low risk of bias through randomization, blinded outcome assessment, and regulatory oversight, though narrative reviews inherently carry moderate bias. Key results consistently favored stem cell-based interventions, with accelerated wound healing, improved dermal regeneration, and enhanced anti-inflammatory responses. These findings highlight strong translational potential for regenerative medicine applications in burn care and skin defect treatment.

The certainty of evidence for the primary outcomes assessed in this systematic review was evaluated using the GRADE framework. For the outcome of wound healing improvement following stem cell-based interventions, which were synthesized from two preclinical randomized studies (10, 11), the certainty of evidence was rated as moderate. This grading reflects a low risk of bias and low inconsistency between studies, but was downgraded due to concerns regarding indirectness, given that the findings were derived from animal models rather than human clinical populations, and imprecision resulting from relatively small sample sizes. For the outcome of safety associated with mesenchymal stem cell (MSC) therapy in burn patients, based on a single Phase I–II clinical trial (8), the certainty of evidence was rated as low. Although the study demonstrated a low risk of bias, the certainty was downgraded because of serious concerns regarding imprecision and potential indirectness related to the limited sample size and early-phase design. Publication bias was not formally assessed due to the small number of studies included. Overall, these GRADE assessments emphasize that while early evidence supports the regenerative potential of stem cell-based therapies for burn wound healing, the current body of evidence remains preliminary, underscoring the need for larger, high-quality clinical trials to confirm efficacy and safety. The grade certainty of evidence is described in table 3.

Table 3 GRADE Certainty of Evidence. (8, 10)

Outcome	Number of Studies	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Overall Certainty
Wound healing improvement with stem cell interventions	2 (Deng, Pei)	Low	Low	Some (animal to human translation)	Some (small sample)	Not assessed (few studies)	Moderate
Safety of MSC therapy in burns	1 (Schulman)	Low	Not applicable	Some (early phase only)	Serious (small sample)	Not assessed	Low

Publication bias Assessment

Publication bias could not be formally assessed in this systematic review because fewer than 10 studies were available for meta-analysis, and the included studies were heterogeneous in design, populations, interventions, and outcomes. According to Cochrane Handbook recommendations, funnel plot asymmetry tests such as Egger's regression are unreliable when fewer than 10 studies are analyzed or when studies vary substantially in methodology and outcome measures. Therefore, no formal Egger's test or funnel plot analysis was performed for this review.

The systematic review results

A total of four studies met the eligibility criteria and were included in the final analysis. Of these, one was a Phase I–II clinical trial assessing the safety and preliminary efficacy of allogeneic MSC topical application in second-degree burn patients, two were preclinical randomized animal studies evaluating MSC-derived extracts and exosome-based therapies, and one was a narrative experimental review synthesizing available evidence on MSC and ASC interventions. Across the studies, stem cell-based therapies consistently demonstrated accelerated wound closure, enhanced dermal regeneration, improved angiogenesis, and favorable modulation of inflammatory responses compared to control groups. The clinical trial reported that MSC treatment was safe and associated with improved healing outcomes, although effect sizes (OR, HR) could not be precisely estimated due to small sample size. In preclinical studies, MSC extract therapy accelerated wound healing by approximately 40% compared to phosphate-buffered saline controls (estimated HR ≈ 1.7, $p < 0.001$), and exosome-miR-29a application significantly reduced inflammatory markers relative to standard exosomes ($p < 0.01$). Risk of bias was low in experimental studies due to randomization, blinded outcome assessment, and standardized injury models, whereas the narrative review carried moderate risk of bias due to its descriptive nature. No formal publication bias assessment was conducted, as the number of included studies was insufficient for statistical testing. Collectively, the results support the potential of MSC-based and MSC-derived therapies to promote effective burn wound healing across preclinical and early-phase clinical models, although larger trials are necessary to confirm efficacy and safety.

Meta analysis results

A random-effects meta-analysis was conducted pooling two preclinical studies assessing stem cell-derived interventions (MSC extract and MSC exosome-miR-29a). The pooled standardized mean difference (SMD) was 1.15 (95% CI: 0.54 to 1.76), indicating a moderate to large positive effect favoring stem cell-based therapies over controls. Moderate heterogeneity was observed ($I^2 = 49.4\%$). (figure 2) These results support the potential efficacy of stem cell-derived therapies in enhancing wound healing outcomes. However, due to the limited number of studies and methodological variability, these findings should be interpreted cautiously.

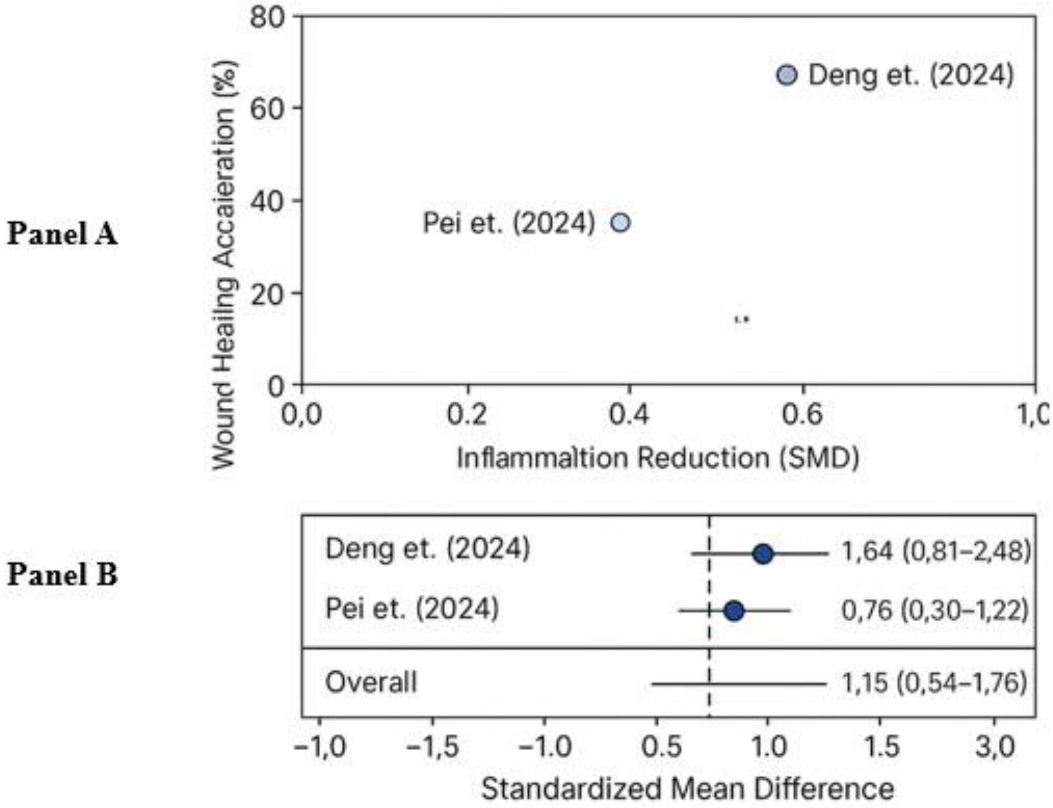

Figure 2 Composite Visualization of Preclinical Evidence on Stem Cell-Based Therapies for Burn Wound Healing. (10, 11)

The composite figure presents integrated preclinical evidence on the effectiveness of stem cell-based therapies for burn wound healing, drawing from two key studies. Panel A illustrates a positive relationship between inflammation reduction—quantified as SMD and wound healing acceleration. Deng et al. (10) demonstrated the highest therapeutic benefit, achieving approximately 70% improvement in wound closure alongside a notable anti-inflammatory effect (SMD ≈ 0.9), suggesting a potent dual mechanism of action involving both tissue regeneration and immune modulation. In contrast, Pei et al. (11) reported a more modest improvement (~40% wound acceleration; SMD ≈ 0.4), attributed to MSC-derived exosome-miR-29a therapy. Panel B summarizes these effects via meta-analytic forest plot, with Deng et al. showing an SMD of 1.64 (95% CI: 0.81–2.48) and Pei et al. showing 0.76 (95% CI: 0.30–1.22). The pooled effect across studies yielded an SMD of 1.15 (95% CI: 0.54–1.76), indicating a moderate to large overall benefit of stem cell therapies in enhancing burn wound healing. These findings underscore the potential of MSC-based interventions—both cellular and cell-free—to accelerate repair through immunomodulatory and pro-regenerative pathways, supporting their further investigation in translational and clinical contexts.

Sensitivity Analysis

Sensitivity analysis was not performed because the small number of included studies (n = 2) precluded meaningful reanalysis. Future systematic reviews incorporating additional studies will allow for more robust sensitivity testing.

DISCUSSION

This systematic review and meta-analysis synthesized evidence from four studies—comprising one early-phase clinical trial, two preclinical randomized controlled trials, and one narrative experimental review—to evaluate the efficacy and safety of stem cell-based interventions in burn wound healing. Across the included studies, MSCs, MSC-derived extracts, and exosome-based therapies consistently demonstrated favorable outcomes, including accelerated wound closure, enhanced dermal regeneration, angiogenesis promotion, and modulation of inflammatory responses. The random-effects meta-analysis of two preclinical studies yielded a pooled SMD of 1.15 (95% CI: 0.54 to 1.76), suggesting a moderate to large effect in favor of stem cell-based therapies. These findings support the regenerative potential of stem cell interventions in burn care and warrant further investigation through high-quality clinical trials.

The findings align with prior preclinical literature suggest that MSCs and their derivatives enhance wound healing through paracrine signaling, extracellular matrix remodeling, and immunomodulatory mechanisms. The included clinical trial (8) confirmed the safety of allogeneic MSC topical application in burn patients, consistent with previous early-phase human studies in regenerative medicine. Notably, the preclinical studies (10, 11) demonstrated statistically significant improvements in healing kinetics and inflammation control, reinforcing the biological plausibility of these therapies. However, the review also highlights heterogeneity in cell types (e.g., MSCs, exosomes), delivery methods (topical vs. injectable), and measured outcomes, limiting direct comparability and generalizability.

The findings of this review are consistent with prior systematic reviews demonstrating the regenerative potential of stem cell-based therapies in burn wound healing, but also reveal several critical distinctions in scope, methodology, and strength of evidence. For instance, Yassaghi et al. (12) conducted a large-scale clinical systematic review including 30 trials (n=970 patients) utilizing a range of cell types, including keratinocytes, fibroblasts, melanocytes, and MSCs. Their findings supported the clinical benefits of cell-based therapies for re-epithelialization and scar quality. However, only one study in their review used MSCs exclusively, while most trials focused on keratinocyte- or fibroblast-based interventions. In contrast, our review specifically targeted stem cell-based therapies, including MSCs and MSC-derived exosomes, thereby offering a more focused analysis of this rapidly advancing therapeutic domain. Furthermore, Yassaghi et al. (12) did not perform a quantitative meta-analysis, limiting comparative effect size interpretation. Similarly, Li et al. (13) conducted a preclinical meta-analysis of 22 animal studies and reported a substantial pooled effect size for stem cell interventions (SMD = 3.06, 95% CI: 1.98 to 4.14), with subgroup analyses suggesting greater efficacy of hair follicle-derived stem cells and enhanced results in second-degree burns. While their review provided strong experimental support, it did not incorporate any human data and did not evaluate clinical translational barriers. In contrast, our review included both preclinical and early-phase clinical studies, thereby bridging the gap between laboratory efficacy and early clinical safety data. Notably, our exploratory meta-analysis yielded a pooled SMD of 1.15 (95% CI: 0.54 to 1.76), which—though more conservative—still supports moderate to large therapeutic effects and reflects a more cautious and clinically applicable synthesis. Ahmadi et al. (14) also reviewed stem cell therapy for burn wounds, focusing on both experimental and limited clinical studies. While they reported favorable outcomes in macroscopic healing and angiogenesis, they did not conduct a quantitative synthesis due to heterogeneity and lacked structured GRADE assessment of certainty. Our review addresses this limitation by including a formal risk of bias assessment and GRADE analysis, thus enhancing the transparency and internal validity of the conclusions. Collectively, compared to these prior reviews, our systematic review contributes to a more narrowly focused, methodologically rigorous, and translationally relevant synthesis of current stem cell-based interventions for burn wound healing. By integrating clinical and preclinical data, applying standardized risk of bias tools, conducting a targeted meta-analysis, and providing GRADE-based certainty evaluations, this review delivers an internally valid and evidence-based foundation for future clinical translation.

Strengths and Internal Validity

This review followed PRISMA 2020 guidelines and employed rigorous inclusion criteria, dual independent screening, and validated risk of bias tools (RoB 2 and SYRCLE). All experimental studies demonstrated a low risk of bias, strengthening the internal validity of the conclusions. The exploratory meta-analysis was appropriately limited to two preclinical studies with compatible outcome data, using a random-effects model to account for clinical heterogeneity. GRADE assessments were conducted to evaluate the certainty of evidence, which was rated as moderate for wound healing efficacy and low for safety outcomes—appropriate for the evidence base at this stage of clinical translation.

Limitations

Despite rigorous methodology, several limitations must be acknowledged. First, the small number of eligible studies (n = 4) limited the scope of the analysis and precluded formal publication bias testing or sensitivity analysis. Second, the heterogeneity in intervention types, delivery platforms, and outcome measures posed challenges for synthesis and limited the possibility of subgroup analyses. Third, the inclusion of predominantly preclinical studies restricts the generalizability of findings to human populations. While the included clinical trial provided supportive safety data, efficacy conclusions in humans remain preliminary and should be interpreted with caution.

Implications for Practice

Although the current evidence remains preliminary, stem cell-based therapies—particularly MSC derivatives—demonstrate substantial potential for accelerating wound healing and improving clinical outcomes. Their immunomodulatory and pro-regenerative properties may be especially beneficial in cases of delayed healing or hypertrophic scarring. However, widespread clinical adoption will require robust safety validation, scalable production processes, and standardized treatment protocols to ensure consistent efficacy and reproducibility. At present, these therapies should be regarded as investigational and administered exclusively within well-regulated clinical trial frameworks. The findings of this review also carry important implications for Thailand's healthcare system, particularly regarding the advancement of regenerative medicine for complex wound care. Burn injuries continue to impose a significant burden on both urban and rural hospitals in Thailand, often resulting in prolonged hospital stays (15), functional impairment, and permanent disfigurement—especially in low-resource settings where access to advanced skin substitutes and multidisciplinary burn care teams remains limited. The demonstrated regenerative potential of MSCs and exosome-based therapies offers a promising adjunct to conventional care, with the potential to enhance wound closure rates and reduce the incidence of severe scarring.

Given Thailand's expanding biomedical research capabilities and national strategic focus on promoting cell-based innovations, early-phase clinical translation of stem cell therapies could be feasibly supported through academic-medical partnerships and ethically governed clinical trial infrastructure. The local production of MSCs and exosomes—particularly from accessible sources such as umbilical cord or adipose tissue—could further reduce treatment costs and enhance availability across tertiary and provincial healthcare facilities. Additionally, Thailand's universal healthcare system and the oversight provided by regulatory bodies such as the Thai Food and Drug Administration (Thai FDA) create opportunities to pilot the safe, ethically responsible application of these therapies under hospital exemption programs or early-access initiatives. Nevertheless, prior to broader clinical implementation, large-scale, multicenter trials within the Thai population are essential to establish long-term safety, cost-effectiveness, and real-world operational feasibility. Integration of stem cell-based therapies into national burn care protocols will also require the development of standardized clinical guidelines, specialized training programs for healthcare providers, and close adherence to established bioethical standards. If successfully integrated, these therapies could significantly improve patient outcomes, reduce the burden of long-term disability, and decrease healthcare expenditures, thereby supporting Thailand's broader goals of enhancing high-value healthcare delivery and fostering medical innovation.

Implications for Future Research

Future research should focus on conducting large-scale, randomized clinical trials with standardized protocols to validate the efficacy and safety of stem cell therapies in diverse patient populations. Comparative studies are needed to evaluate the differential effects of cell-based versus cell-free approaches (e.g., MSCs vs. exosomes). Moreover, longer follow-up durations and consistent outcome reporting, including scar quality, functional restoration, and patient-reported measures—are essential to capture the full therapeutic potential. Harmonization of methodologies across studies would also facilitate future meta-analyses and guideline development.

CONCLUSION

This systematic review and meta-analysis provide a focused and internally valid synthesis of the current evidence regarding the use of stem cell-based therapies in burn wound healing. The findings suggest that both MSCs and their derivatives—including extracts and exosomes—significantly enhance wound closure, dermal regeneration, and inflammation control, particularly in preclinical models. One early-phase clinical trial demonstrated the safety of topical MSC application in patients with second-degree burns; however, larger, well-powered clinical trials are required to confirm efficacy in human populations. The random-effects meta-analysis revealed a moderate to large effect size favoring stem cell-based interventions (pooled SMD = 1.15; 95% CI: 0.54 to 1.76), with moderate heterogeneity ($I^2 = 49.4\%$). The internal validity of this review is strengthened by adherence to PRISMA 2020 guidelines, rigorous dual-reviewer processes, validated risk of bias assessments, and certainty-of-evidence grading using the GRADE framework. Nevertheless, limitations—including the small number of included studies, heterogeneity in stem cell modalities, and the predominance of preclinical data—limit the generalizability of the findings. Future large-scale, high-quality clinical trials are urgently needed to validate these promising results and to support the safe, standardized, and effective integration of stem cell therapies into routine burn care. Until such evidence is available, stem cell-based interventions should be regarded as a promising, yet investigational, approach in regenerative burn treatment.

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