Efficacy and Safety of Stem Cell Therapy for Spinal Cord Injury in Adults: A Systematic Review and Meta-Analysis

Anadya Rhadika[1*], Sultan Adhitya Romano[2], Himawan Widyatmiko[3], Andrew Wilbert Tanuwijaya[4], Putu Surya Pradipta Hariantha Putra[5], Salma Rizqi Amanah[6], Abdelrahman Ramadan Elashry[7], Sarmad Javaid[8], Made Agus Mahendra Inggas[9], Jeremiah Hilkiah Wijaya[10]

[1] RS Pusat Otak Nasional, Jakarta, Indonesia
[2] Universitas YARSI, Jakarta, Indonesia
[3] Emergency Department, RSUD Pandega Pangandaran, West Java, Indonesia
[4] Fakultas Kedokteran dan Ilmu Kesehatan, Universitas Katolik Indonesia Atma Jaya, Jakarta, Indonesia
[5] Universitas Udayana, Bali, Indonesia
[6] Universitas Pembangunan Nasional Veteran Jakarta, Jakarta, Indonesia
[7] College of Medicine, University of Sharjah, Sharjah, UAE
[8] Sharif Medical and Dental College, Lahore, Pakistan
[9] Department of Neurosurgery, Universitas Pelita Harapan, Tangerang, Banten, Indonesia
[10] School of Public Health and Preventive Medicine, Monash University, Melbourne, Victoria, Australia

Citation : Rhadika A, Romano SA, Widyatmiko H, Tanuwijaya AW, Hariantha Putra PSP, Amanah SR, Elashry AR, Javaid S, Inggas MAM, Wijaya JH. Efficacy and Safety of Stem Cell Therapy for Spinal Cord Injury in Adults: A Systematic Review and Meta-Analysis. Medicinus. 2025 October;15(1):66-80.
Keywords: Spinal cord injury; stem cell therapy; neuroregeneration; mesenchymal stem cells; AIS improvement.
Correspondance : Anadya Rhadika
E-mail : anadyardk@gmail.com
Online First : October 2025

Abstract

Background: Despite encouraging early results, clinical outcomes remain inconsistent across trials. This study aimed to systematically evaluate the efficacy and safety of stem cell therapy in adults with spinal cord injury (SCI).

Methods: A systematic review and meta-analysis were conducted following PRISMA 2020 guidelines. PubMed, EMBASE, and Scopus were searched until 18 October 2025. Eligible studies included adult SCI patients receiving stem cell therapy with measurable neurological outcomes. Data synthesis was performed using Review Manager 5.4 under a random-effects model, reporting pooled risk ratios (RR) with 95% confidence intervals (CIs). Risk of bias was assessed using ROBINS-I, and evidence certainty was graded via GRADE.

Result: Thirteen studies involving 470 participants (286 intervention, 184 control) were included. Stem cell therapy significantly improved neurological recovery compared with controls (RR = 2.64; 95% CI 1.70–4.10; $p < 0.0001$; $I^2 = 0\%$). Subgroup analyses showed consistent benefits across baseline AIS classifications (RR = 2.61; 95% CI 1.71–3.98) and cell doses (RR = 2.75; 95% CI 1.63–4.64). No major safety signals were identified. GRADE assessment rated the certainty of efficacy evidence as moderate.

Conclusions: Stem cell therapy yields significant neurological improvement in adult SCI with a favorable safety profile. The findings support its regenerative potential through neuroprotective and remyelinating mechanisms. However, larger randomized controlled trials are required to validate efficacy, optimize protocols, and assess long-term safety.

Introduction

Stem cell therapy has emerged as a promising regenerative approach for spinal cord injury (SCI), a condition that results in irreversible neurological deficits due to the limited intrinsic repair capacity of the central nervous system.[1] The rationale for using stem cells lies in their ability to differentiate into neural lineages, secrete neurotrophic factors, and modulate the

hostile post-injury microenvironment that inhibits axonal regrowth.[1,2] Unlike pharmacologic or surgical interventions that primarily aim to limit secondary damage, stem cells offer a biological means to restore neural circuitry, promote remyelination, and enhance functional recovery. Such potential has driven extensive experimental and clinical interest in translating stem cell–based therapies into viable treatments for SCI.[3]

Over the past two decades, multiple clinical trials have evaluated various stem cell types—most notably mesenchymal stem cells (MSCs), neural stem/progenitor cells (NSPCs), and induced pluripotent stem cells (iPSCs)—for their safety and regenerative efficacy.[4] While some studies have reported improvements in sensory and motor scores, outcomes remain heterogeneous, with inconsistent methodologies, variable injury levels, and differing routes and timing of cell administration.[5–7] Moreover, long-term safety concerns such as immune reactions, ectopic tissue formation, and tumorigenicity continue to limit widespread clinical application. The lack of standardized protocols and robust evidence synthesis has created uncertainty regarding the true clinical benefit of stem cell therapy in adults with SCI.[8]

The physiological complexity of SCI involves both primary mechanical insult and secondary injury mechanisms, including ischemia, excitotoxicity, inflammation, and glial scar formation, all of which impede endogenous regeneration.[9] Stem cell therapy aims to counteract these processes by replacing lost neurons and oligodendrocytes, secreting anti-inflammatory cytokines, and promoting neuroplasticity within spared neural networks.[10] Given the growing but fragmented body of evidence, a systematic and quantitative assessment is crucial to clarify clinical outcomes and safety profiles. This study therefore aims to conduct a systematic review and meta-analysis to evaluate the efficacy and safety of stem cell therapy for spinal cord injury in adults.

Material And Methods

This systematic review included studies that assessed the efficacy and safety of stem cell therapy in adult patients aged 18 years or older with spinal cord injury (SCI), regardless of the injury's level or severity. Eligible study designs comprised randomized controlled trials (RCTs), non-randomized controlled studies, and prospective cohort studies that reported at least one measurable functional, neurological, or safety outcome. Excluded studies included case reports, animal studies, reviews, and conference abstracts lacking sufficient data.

A comprehensive literature search was performed across PubMed, EMBASE,

and Scopus from their inception until 18 October 2025. To ensure thoroughness, the reference lists of included studies and relevant reviews were manually screened to identify additional eligible publications. The search strategy employed both Medical Subject Headings (MeSH) and free-text terms associated with “spinal cord injury,” “stem cell therapy,” “transplantation,” and “regeneration,” with Boolean operators and database-specific filters applied to optimize retrieval.

The study selection process involved independent screening of titles and abstracts by all reviewers, followed by full-text assessments to confirm eligibility. Any disagreements were resolved through discussion and consensus, ensuring methodological consistency. This process adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines.[11] Data extraction was conducted independently by two reviewers using a standardized form, which captured key study characteristics such as authorship, publication year, design, sample size, participant demographics, stem cell type and source, route and timing of administration, follow-up duration, and outcome measures.

Primary outcomes of interest included functional and neurological improvements, commonly evaluated through the American Spinal Injury Association (ASIA) Impairment Scale (AIS) or equivalent motor and sensory scores. Secondary outcomes encompassed adverse events, complication rates, and mortality. Additional data regarding intervention characteristics, such as cell type, dosage, delivery method, and study funding sources were also systematically recorded.

The risk of bias in each study was evaluated using the ROBINS-I (Risk of Bias in Non-Randomized Studies of Interventions) tool across seven domains. Independent assessments by all reviewers were reconciled through discussion to ensure reliability. For effect measures, all outcomes were treated as dichotomous data and expressed as Risk Ratios (RRs) with corresponding 95% confidence intervals (CIs), facilitating standardized comparisons across studies.

Data synthesis was performed through meta-analysis using Review Manager (RevMan) version 5.4. A random-effects model (DerSimonian–Laird method) with the Mantel–Haenszel approach was applied for dichotomous outcomes, while the Restricted Maximum Likelihood (REML) method was used for continuous data. Statistical heterogeneity was quantified using the I^2 statistic, and significance was set at $p < 0.05$. Forest plots were generated to illustrate pooled effect estimates, and funnel plots were used to assess publication bias. Sensitivity analyses tested the robustness of results.

Publication bias was visually examined via funnel plots and statistically assessed using Egger's regression test for outcomes with at least ten studies. Finally, the overall quality and certainty of evidence were appraised using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) framework. Evidence was categorized as high, moderate, low, or very low depending on risk of bias, inconsistency, indirectness, imprecision, and potential publication bias.

Result

Work should be reported in SI units. Undue repetition in text and tables should be avoided. Comment on validity and significance of results is appropriate but broader discussion of their implication is restricted to the next section. Subheadings that aid clarity of presentation within this and the previous section are encouraged.

The purpose of the Results is to state your findings and make interpretations and/or opinions, explain the implications of your findings, and make suggestions for future research. The main function is to answer the questions posed in the introduction, explain how the results support the answers and, how the answers fit in with existing knowledge on the topic. The Discussion is considered the heart of the paper and usually requires several writing attempts.

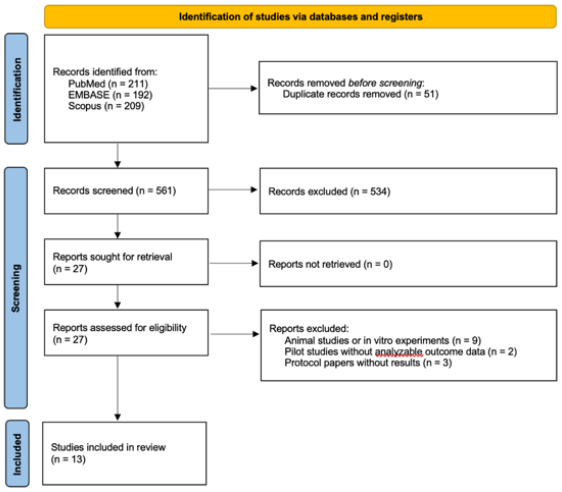


Figure 1. PRISMA diagram of the study selection process

A total of 612 records were initially identified from the databases, including PubMed (n = 211), EMBASE (n = 192), and Scopus (n = 209). After the removal of 51 duplicate records, 561 unique studies were screened by title and abstract. Of these, 534 records were excluded for not meeting the eligibility criteria. Twenty-seven full-text articles were assessed for eligibility, and none were excluded due to retrieval issues. Following full-text review, nine studies were excluded for being animal or in vitro experiments, two were excluded as pilot studies without analyzable outcome data, and three were protocol papers without results. Ultimately, 13 studies met the inclusion criteria and were included in the final systematic review and meta-analysis (Figure 1).[5,7,12–22]

The risk of bias assessment using the ROBINS-I tool demonstrated that most included studies exhibited a low risk of

bias across the seven evaluated domains, particularly regarding confounding factors and participant selection (Figure 2). A few studies presented moderate risk primarily due to missing data, classification of interventions, or incomplete outcome reporting.

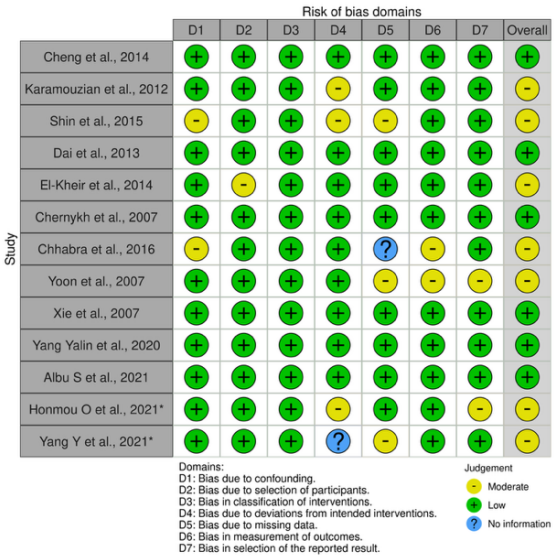


Figure 2. Risk of bias of eligible studies using ROBINS-I

Table 1. Demographic characteristics of included studies.

Study (Author, Year)	Country	Participants (SCT / Control)	Mean or Range of Age (yrs)	Injury Level (SCT / Control)	Preinjury Grade (AIS)	Stem Cell Source	Cell Quantity	Delivery Technique
Cheng et al., 2014	China	10 / 14	35.25	Thoracolumbar / –	AIS A	Umbilical cord MSCs	4×10^{7}	Local lesion injection
Karamouzian et al., 2012	Iran	11 / 20	33.4	Thoracic / Thoracic	AIS A	Bone marrow MSCs	7×10^{5} – 1.2×10^{6}	Lumbar puncture
Shin et al., 2015	Korea	19 / 15	37.2	Cervical / Cervical	AIS A–B	Human neural stem/progenitor cells	10^{8}	Direct lesion injection
Dai et al., 2013	China	20 / 20	34.9	Cervical / Cervical	AIS A	Bone marrow MSCs	2×10^{7}	Lesion site injection
El-Kheir et al., 2014	Egypt	50 / 20	16–45	10 cervical & 40thoracic / 7 crvical & 13 thoracic	AIS A or B	Bone marrow MSCs	2×10^{6} per kg	Lumbar puncture
Chernykh et al., 2007	Russia	18 / 18	32.4	Cervical, thoracic, lumbar (varied)	AIS A	Bone marrow mononuclear cells	NR	Injection into cystic cavity & IV
Chhabra et al., 2016	India	14 / 7	24.9	Thoracic / Thoracic	AIS A	Bone marrow MSCs	7×10^{8} – 10^{9}	Lumbar puncture or lesion injection
Yoon et al., 2007	Korea	35 / 13	41.3	23 cervical, 12 thoracic / 7 cervical, 6 thoracic	AIS A	Bone marrow MSCs	1.98×10^{8}	Injection into lesion
Xie et al., 2007	China	11 / 13	18–49 (SCT), 21–53 (Ctrl)	Cervical, thoracic, lumbar / similar	AIS A–D	Bone marrow MSCs	$2–5\times10^{9}$	Lumbar puncture
Yang Yalin et al., 2020	China	34 / 34	27–43	44 Cervical/24 Thoracic	AIS A–D	Autologous bone marrow		Intrathecal
Albu S et al., 2021	Spain	10 / 10	25–47	Thoracic	AIS A–D	Allogeneic umbilical cord cells		Intrathecal
Honmou O et al., 2021*	Japan	13 / –	21–66	Cervical	AIS A–D	Autologous bone marrow		Intravenous
Yang Y et al., 2021*	China	41 / –	18–65	24 Cervical/ 7 Thoracic/10 Dorsal-lumbar	AIS A–D	Allogeneic umbilical cord cells		Intrathecal

*Single arm clinical trial

Table 2. GRADE summary of findings.

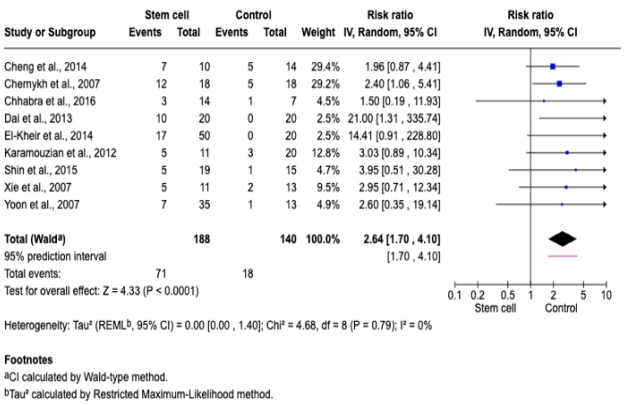
Outcome (follow-up)	Participants (studies)	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Overall certainty (GRADE)	Relative effect	Absolute effect (per 100 pts)*
AIS grade improvement (overall) (longest available)	532 (13)	Mostly non-randomized comparative studies	Not serious†	Not serious (I^2=0%)	Not serious (adults with SCI)	Not serious (95% CI excludes no effect)	MODERATE ⨁⨁⨁◯	RR 2.64 (95% CI 1.70–4.10) (Figure 3)	+21 more/100 improved (from +9 to +40 more) — assuming a 13/100 control risk from Figure 3
AIS grade improvement by baseline AIS (A vs B/C)	532 (13)	Mostly non-randomized	Not serious†	Not serious (I^2=0% within subgroups)	Not serious	Not serious	MODERATE ⨁⨁⨁◯	RR 2.61 (1.71–3.98) (Figure 4)	From a 13/100 control risk: +21 more/100 (from +9 to +38 more)
AIS grade improvement by cell dose (10^6, 10^7, 10^8 cells)	492 (11)	Mostly non-randomized	Not serious†	Not serious (I^2=0%; no subgroup diffs)	Not serious	Not serious	MODERATE ⨁⨁⨁◯	RR 2.75 (1.63–4.64) (Figure 5)	From a 13/100 control risk: +23 more/100 (from +8 to +47 more)

A total of 286 participants received stem cell therapy (SCT) and 184 participants served as controls across the 13 included studies. The studies were conducted in Asia (China, Korea, Japan, India), Europe (Spain), Russia, and Egypt, reflecting a diverse geographic representation. The mean or range of participant ages varied between 16 and 66 years, indicating that most studies focused on adult populations with both acute and chronic spinal cord injuries. The majority of participants had cervical or thoracic injuries, with baseline preinjury AIS grades ranging from A to D, although most were complete injuries (AIS A).

The predominant stem cell sources were bone marrow–derived MSCs (used in 8 studies), followed by umbilical cord–derived MSCs (2 studies), allogeneic umbilical cord cells (2 studies), and neural stem/progenitor cells (1 study). The delivery methods varied across studies: lumbar puncture/intrathecal injection was the most common route (7 studies), while others used direct lesion site injections, intravenous infusion, or combined approaches (e.g., intralesional and intravenous). Reported cell quantities ranged widely from 7×10^5 to 5×10^9 cells, with some studies expressing dosage relative to body weight (e.g., 2×10^6 cells/kg).

Meta-analysis

The overall pooled meta-analysis demonstrated a statistically significant improvement in AIS grading following stem cell therapy compared with control treatment (RR = 2.64, 95% CI: 1.70–4.10, $p < 0.0001$; $I^2 = 0\%$) (Figure 3). Subgroup analysis according to baseline AIS classification also showed a significant overall effect (RR = 2.61, 95% CI: 1.71–3.98, $p < 0.0001$; $I^2 = 0\%$) across both AIS A and AIS B/C groups (Figure 4). When stratified by administered cell quantity, the pooled estimate remained significant (RR = 2.75, 95% CI: 1.63–4.64, $p = 0.0002$; $I^2 = 0\%$) (Figure 5). Across all analyses, no significant heterogeneity was observed ($\tau^2 = 0.00$; $\chi^2 = 4.68$, df = 8, $p = 0.79$ for the main model), and the funnel plots demonstrated symmetry, indicating a low likelihood of publication bias.



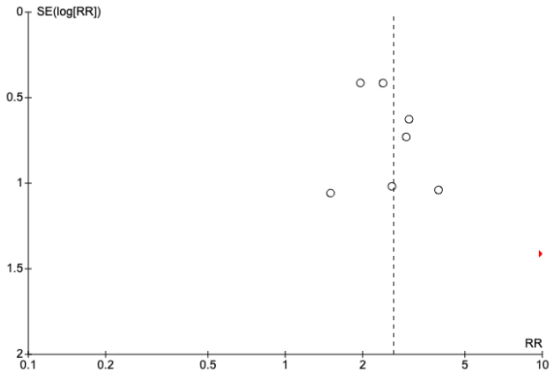
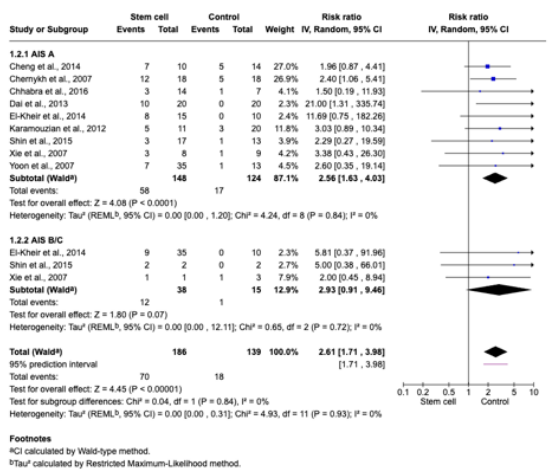


Figure 3. Pooled meta-analysis of improvement rates in AIS grading following stem cell therapy.



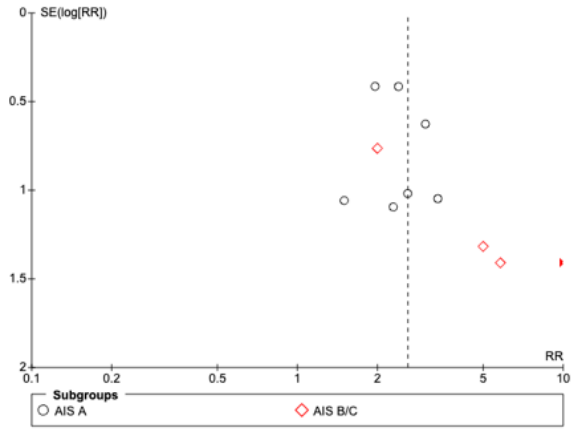
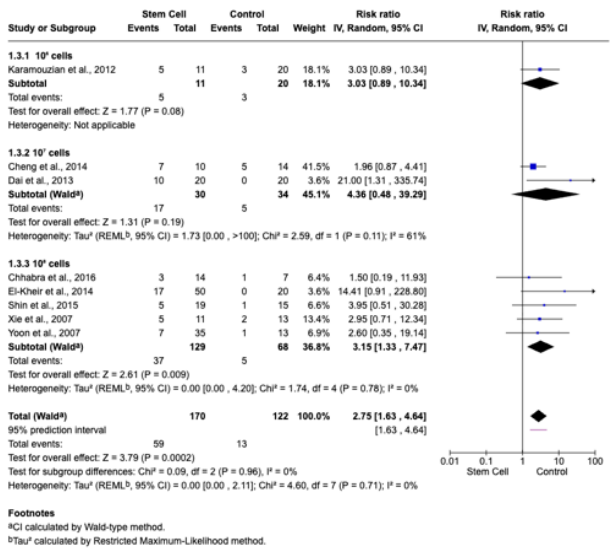


Figure 4. Subgroup meta-analysis comparing AIS grade improvement between stem cell therapy and control groups across different baseline AIS classifications.



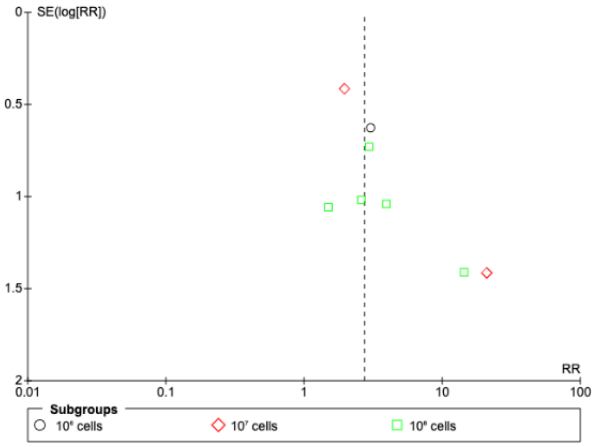


Figure 5. Subgroup meta-analysis comparing AIS grade improvement between stem cell therapy and control groups according to varying administered cell doses.

GRADE Certainty Assessment

The GRADE assessment (table 2) indicated moderate certainty of evidence for the efficacy of stem cell therapy in improving neurological outcomes among adults with spinal cord injury. Evidence consistency and low heterogeneity supported upgrading from low to moderate certainty, despite the predominance of non-randomized studies. In contrast, the certainty of evidence for safety outcomes was rated very low because of limited

data, inconsistent reporting, and potential bias in adverse event documentation.

Discussion

The nature and findings of the study are placed in context of other relevant published data. The present meta-analysis demonstrated a significant improvement in neurological recovery among adult patients with SCI who received stem cell therapy compared with controls (RR = 2.64, 95% CI: 1.70–4.10, p < 0.0001). Subgroup analyses revealed consistent effects across different baseline AIS classifications (RR = 2.61) and cell dose groups (RR = 2.75), with minimal heterogeneity (I^2 = 0%) across studies. These findings suggest a robust and reproducible therapeutic effect of stem cell transplantation for promoting functional improvement following SCI. The consistency of effect sizes across subgroups implies that stem cell therapy benefits may be relatively independent of baseline severity or administered cell quantity, underscoring its potential as a broadly applicable regenerative intervention.

Several studies in related neurological conditions support the efficacy of stem cell therapy in enhancing neural recovery, lending further weight to the current findings.[23,24] For instance, meta-analyses in ischemic stroke and traumatic brain injury have similarly demonstrated significant improvements in functional outcomes following MSCs administration, with effect estimates comparable to those observed in SCI populations.[25,26] However, conflicting evidence exists; some trials in chronic SCI reported limited or transient functional recovery, likely due to the extensive gliosis and scar tissue that restrict cellular integration. These mixed outcomes across diseases and time points highlight that while stem cells possess regenerative potential, their efficacy may be modulated by injury chronicity, host immune responses, and local microenvironmental factors.

The beneficial effects of stem cell therapy can be attributed to several mechanisms. Following SCI, primary mechanical insult initiates a cascade of secondary injury processes, including ischemia, excitotoxicity, inflammation, and glial scar formation, which collectively impair axonal conduction and neuronal survival.[27] Transplanted stem cells—particularly MSCs and neural progenitors—can mitigate these effects by secreting neurotrophic factors such as brain-derived neurotrophic factor (BDNF) and glial cell line–derived neurotrophic factor (GDNF), promoting angiogenesis, and modulating the immune response toward a reparative phenotype.[28–30] Moreover, some stem cells may differentiate into oligodendrocytes or neurons, contributing to remyelination and restoration of neural circuitry.[29] This neuroprotective and neuroregenerative

synergy underlies the physiological plausibility of the observed clinical improvements.[30]

Despite encouraging results, several limitations and translational challenges remain. The included studies displayed variability in stem cell sources, delivery routes, and dosing protocols, which may influence therapeutic efficacy and safety. The long-term survival, differentiation, and integration of transplanted cells within the spinal cord remain uncertain, raising theoretical concerns regarding tumorigenicity and ectopic tissue formation. Furthermore, the pharmacological microenvironment of the injured spinal cord—characterized by persistent inflammation, oxidative stress, and inhibitory extracellular matrix molecules—can hinder stem cell viability and function. Future research should therefore focus on optimizing cell type selection, timing of administration, and combination therapies (e.g., growth factors or biomaterial scaffolds) to enhance cell survival, integration, and functional outcomes.

Study Limitations

Several limitations should be acknowledged when interpreting the findings of this meta-analysis. First, most included studies were non-randomized clinical trials with small sample sizes, introducing potential selection and performance biases despite overall low risk scores under the ROBINS-I tool. Second, there was heterogeneity in study protocols, including differences in stem cell sources, doses, delivery routes, and follow-up durations, which may influence treatment outcomes and complicate direct comparison. Third, most trials lacked long-term follow-up data, limiting assessment of the durability and safety of neurological improvements. Fourth, despite the use of random-effects modeling, publication bias cannot be fully excluded, as negative or null studies are less likely to be reported. Lastly, variability in outcome assessment tools, such as differences in AIS scoring criteria or assessor blinding, may have introduced subjective bias in evaluating neurological improvement.

Conclusion

This systematic review and meta-analysis demonstrated that stem cell therapy significantly improves neurological recovery in adults with spinal cord injury, with consistent benefits observed across injury severity and cell dose subgroups. The pooled evidence supports the potential of stem cell–based interventions as an effective regenerative approach for spinal cord repair, likely mediated by neuroprotective, anti-inflammatory, and remyelinating mechanisms. However, the certainty of evidence remains moderate, primarily due to methodological limitations and heterogeneous study designs. Further large-scale, randomized controlled trials

with standardized protocols and long-term follow-up are warranted to confirm therapeutic efficacy, establish optimal treatment parameters, and ensure safety before widespread clinical adoption.

Acknowledgment

None.

References

1. Zeng CW. Advancing Spinal Cord Injury Treatment through Stem Cell Therapy: A Comprehensive Review of Cell Types, Challenges, and Emerging Technologies in Regenerative Medicine. Int J Mol Sci. 2023 Sept 20;24(18):14349. https://doi.org/10.3390/ijms241814349
2. Kawai M, Nagoshi N, Okano H, Nakamura M. A review of regenerative therapy for spinal cord injury using human iPS cells. North American Spine Society Journal (NASSJ). 2023 Mar;13:100184. https://doi.org/10.1016/j.xnsj.2022.100184
3. Kataria S, Patel U, Yabut K, Patel J, Patel R, Patel S, et al. Recent Advances in Management of Neuropathic, Nociceptive, and Chronic Pain: A Narrative Review with Focus on Nanomedicine, Gene Therapy, Stem Cell Therapy, and Newer Therapeutic Options. Curr Pain Headache Rep. 2024 May;28(5):321–33. https://doi.org/10.1007/s11916-024-01227-5
4. Xiao J, Yang R, Biswas S, Qin X, Zhang M, Deng W. Mesenchymal Stem Cells and Induced Pluripotent Stem Cells as Therapies for Multiple Sclerosis. IJMS. 2015 Apr 24;16(5):9283–302. https://doi.org/10.3390/ijms16059283
5. Protain HJ, Kutzler MA, Valentine BA. Assessment of cytologic evaluation of preputial epithelial cells as a diagnostic test for detection of adrenocortical disease in castrated ferrets. Am J Vet Res. 2009 May;70(5):619–23. https://doi.org/10.2460/ajvr.70.5.619
6. Thanaskody K, Jusop AS, Tye GJ, Wan Kamarul Zaman WS, Dass SA, Nordin F. MSCs vs. iPSCs: Potential in therapeutic applications. Front Cell Dev Biol. 2022;10:1005926. https://doi.org/10.3389/fcell.2022.1005926
7. Zun-wei X, Gui-xiang C, Yi-zhao L. Curative effect of autologous mesenchymal stem cell transplantation on spinal cord injury. Zhongguo Zuzhi Gongcheng Yanjiu yu Linchuang Kangfu. 2007;11(7):1277-1279.
8. Huang L, Fu C, Xiong F, He C, Wei Q. Stem Cell Therapy for Spinal Cord Injury. Cell Transplant. 2021;30:963689721989266. https://doi.org/10.1177/0963689721989266
9. Anwar MA, Al Shehabi TS, Eid AH. Inflammogenesis of Secondary Spinal Cord Injury. Front Cell Neurosci. 2016;10:98. https://doi.org/10.3389/fncel.2016.00098

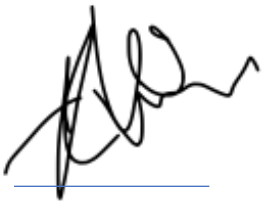
10. Darehbagh RR, Seyedoshohadaei SA, Ramezani R, Rezaei N. Stem cell therapies for neurological disorders: current progress, challenges, and future perspectives. Eur J Med Res. 2024 July 25;29(1):386. https://doi.org/10.1186/s40001-024-01987-1
11. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021 Mar 29;372(n71):1-9. https://doi.org/10.1136/bmj.n71
12. Albu S, Kumru H, Coll R, Vives J, Vallés M, Benito-Penalva J, et al. Clinical effects of intrathecal administration of expanded Wharton jelly mesenchymal stromal cells in patients with chronic complete spinal cord injury: a randomized controlled study. Cytotherapy. 2021 Feb;23(2):146–56. https://doi.org/10.1016/j.jcyt.2020.08.008
13. Cheng H, Liu X, Hua R, Dai G, Wang X, Gao J, et al. Clinical observation of umbilical cord mesenchymal stem cell transplantation in treatment for sequelae of thoracolumbar spinal cord injury. J Transl Med. 2014 Sept 12;12:253. https://doi.org/10.1186/s12967-014-0253-7
14. Chernykh ER, Stupak VV, Muradov GM, Sizikov MY, Shevela EY, Leplina OY, et al. Application of autologous bone marrow stem cells in the therapy of spinal cord injury patients. Bull Exp Biol Med. 2007 Apr;143(4):543–7. https://doi.org/10.1007/s10517-007-0175-y
15. Chhabra HS, Sarda K, Arora M, Sharawat R, Singh V, Nanda A, et al. Autologous bone marrow cell transplantation in acute spinal cord injury--an Indian pilot study. Spinal Cord. 2016 Jan;54(1):57–64. https://doi.org/10.1038/sc.2015.134
16. Dai G, Liu X, Zhang Z, Yang Z, Dai Y, Xu R. Transplantation of autologous bone marrow mesenchymal stem cells in the treatment of complete and chronic cervical spinal cord injury. Brain Res. 2013 Oct 2;1533:73–9. https://doi.org/10.1016/j.brainres.2013.08.016
17. El-Kheir WA, Gabr H, Awad MR, Ghannam O, Barakat Y, Farghali HAMA, et al. Autologous bone marrow-derived cell therapy combined with physical therapy induces functional improvement in chronic spinal cord injury patients. Cell Transplant. 2014 Apr;23(6):729–45. https://doi.org/10.3727/096368913x664540
18. Honmou O, Yamashita T, Morita T, Oshigiri T, Hirota R, Iyama S, et al. Intravenous infusion of auto serum-expanded autologous mesenchymal stem cells in spinal cord injury patients: 13 case series. Clinical Neurology and Neurosurgery. 2021 Apr;203:106565. https://doi.org/10.1016/j.clineuro.2021.106565
19. Karamouzian S, Nematollahi-Mahani SN, Nakhaee N, Eskandary H. Clinical safety and primary efficacy of bone marrow mesenchymal cell transplantation in subacute spinal cord injured patients. Clin Neurol Neurosurg. 2012 Sept;114(7):935–9. https://doi.org/10.1016/j.clineuro.2012.02.003

20. Shin JC, Kim KN, Yoo J, Kim IS, Yun S, Lee H, et al. Clinical Trial of Human Fetal Brain-Derived Neural Stem/Progenitor Cell Transplantation in Patients with Traumatic Cervical Spinal Cord Injury. Neural Plast. 2015;2015:630932. https://doi.org/10.1155/2015/630932
21. Yang Y, Pang M, Du C, Liu ZY, Chen ZH, Wang NX, et al. Repeated subarachnoid administrations of allogeneic human umbilical cord mesenchymal stem cells for spinal cord injury: a phase 1/2 pilot study. Cytotherapy. 2021 Jan;23(1):57–64. https://doi.org/10.1016/j.jcyt.2020.09.012
22. Yoon SH, Shim YS, Park YH, Chung JK, Nam JH, Kim MO, et al. Complete spinal cord injury treatment using autologous bone marrow cell transplantation and bone marrow stimulation with granulocyte macrophage-colony stimulating factor: Phase I/II clinical trial. Stem Cells. 2007 Aug;25(8):2066–73. https://doi.org/10.1634/stemcells.2006-0807
23. Nguyen H, Zarriello S, Coats A, Nelson C, Kingsbury C, Gorsky A, et al. Stem cell therapy for neurological disorders: A focus on aging. Neurobiol Dis. 2019 June;126:85–104. https://doi.org/10.1016/j.nbd.2018.09.011
24. Tang X, Deng P, Li L, He Y, Wang J, Hao D, et al. Advances in genetically modified neural stem cell therapy for central nervous system injury and neurological diseases. Stem Cell Res Ther. 2024 Dec 18;15(1):482. https://doi.org/10.1186/s13287-024-04089-1
25. Zanier ER, Pischiutta F, Rulli E, Vargiolu A, Elli F, Gritti P, et al. MesenchymAl stromal cells for Traumatic bRain Injury (MATRIx): a study protocol for a multicenter, double-blind, randomised, placebo-controlled phase II trial. Intensive Care Med Exp. 2023 Aug 25;11(1):56. https://doi.org/10.1186/s40635-023-00535-1
26. Shen Z, Tang X, Zhang Y, Jia Y, Guo X, Guo X, et al. Efficacy and safety of mesenchymal stem cell therapies for ischemic stroke: a systematic review and meta-analysis. Stem Cells Transl Med. 2024 Sept 10;13(9):886–97. https://doi.org/10.1093/stcltm/szae040
27. Chopra M, Kumar H. Navigating the complexities of spinal cord injury: an overview of pathology, treatment strategies and clinical trials. Drug Discovery Today. 2025 June;30(6):104387. https://doi.org/10.1016/j.drudis.2025.104387
28. Kaminska A, Radoszkiewicz K, Rybkowska P, Wedzinska A, Sarnowska A. Interaction of Neural Stem Cells (NSCs) and Mesenchymal Stem Cells (MSCs) as a Promising Approach in Brain Study and Nerve Regeneration. Cells. 2022 Apr 26;11(9):1464. https://doi.org/10.3390/cells11091464
29. Hsu YC, Lee DC, Chiu IM. Neural Stem Cells, Neural Progenitors, and Neurotrophic Factors. Cell Transplant. 2007 Feb;16(2):133–50. Available from: https://pubmed.ncbi.nlm.nih.gov/17474295/

30. De Gioia R, Biella F, Citterio G, Rizzo F, Abati E, Nizzardo M, et al. Neural Stem Cell Transplantation for Neurodegenerative Diseases. IJMS. 2020 Apr 28;21(9):3103. https://doi.org/10.3390/ijms21093103

Author's Statement

The authors declared that all the images and figures in this manuscript is/are author's own work and/or has obtained necessary permission to re-use the content from the authors and publisher of respective materials.



(Anadya Rhadika)