INPLASY

Current Preclinical and Clinical Evidence of Shock Wave Therapy for Spinal Cord Injury: A Systematic Review

INPLASY202630053
doi: 10.37766/inplasy2026.3.0053
Received: 15 March 2026
Published: 15 March 2026

Nagele, S; Zellmer, B; Graber, M; Winter-Pölzl, L; Engler, C; Hirsch, J; Schmidt, S; Eder, J; Lohmann, R; Ioannou-Nikolaidou, M; Heim, V; Grimm, M; Bonaros, N; Gollmann-Tepeköylü, C; Holfeld, J; Nägele, F.

Corresponding author:
Felix Naegele

felix.naegele@i-med.ac.at

Author Affiliation:
Medical University of Innsbruck.

ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202630053

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 15 March 2026 and was last updated on 15 March 2026.

INTRODUCTION

Review question / Objective The objective of this systematic review is to evaluate the current preclinical and clinical evidence on the use of extracorporeal shock wave therapy (SWT) as a regenerative treatment for spinal cord injury (SCI). Specifically, the review aims to assess whether SWT improves functional recovery and promotes regenerative biological processes in experimental and clinical SCI models, as well as to summarize its safety, feasibility, and potential therapeutic mechanisms.

Condition being studied Spinal cord injury (SCI) is a severe neurological condition resulting from traumatic or ischemic damage to the spinal cord, often leading to partial or complete loss of motor, sensory, and autonomic function below the level of the lesion. SCI is associated with substantial morbidity, long-term disability, and significant socioeconomic burden. Following the primary mechanical injury, a complex secondary injury cascade involving ischemia, inflammation, oxidative stress, and apoptotic pathways contributes to progressive neuronal damage and limited functional recovery. Despite advances in acute care and rehabilitation, effective regenerative therapies remain limited, highlighting the need for novel treatment strategies aimed at promoting neural repair and functional recovery.

METHODS

Participant or population This review includes studies investigating spinal cord injury (SCI) in both human patients and experimental models. Clinical populations include individuals with acute traumatic SCI, spinal cord ischemia, or chronic paraplegia. Preclinical studies include animal models (rats, mice, zebrafish) as well as in vitro and ex vivo neural tissue or cell models used to investigate the regenerative effects of treatment following SCI.

Intervention The intervention of interest is extracorporeal shock wave therapy (SWT) applied to the spinal cord region surrounding the injury

site. SWT is a non-invasive regenerative treatment modality intended to promote neural repair, angiogenesis, and neuroprotective mechanisms following spinal cord injury.

Comparator Comparators include untreated control groups, sham-treated groups, or baseline measurements prior to intervention, depending on the design of the included studies.

Study designs to be included Eligible studies include preclinical experimental studies (in vivo, in vitro, or ex vivo) and clinical interventional studies, including prospective trials and randomized controlled trial protocols. Case reports, review articles, and studies not investigating regenerative applications of shock wave therapy in SCI were excluded.The review included preclinical experimental studies (in vivo, in vitro, and ex vivo models) and clinical interventional studies, including prospective trials and randomized controlled trial protocols. Case reports, review articles, non-regenerative SWT applications, and.

Eligibility criteria Studies were eligible for inclusion if they met the following criteria: (1) original research articles published in peer-reviewed journals between 2000 and 2025, (2) written in English, and (3) investigating the therapeutic use of extracorporeal shock wave therapy (SWT) in spinal cord injury (SCI). Both preclinical experimental studies (including in vivo animal models, in vitro studies, and ex vivo tissue studies) and clinical interventional studies were considered eligible.

Studies were excluded if they were case reports, review articles, studies not applying shock wave therapy as a regenerative treatment for SCI, studies focusing on other therapeutic targets, or studies published outside the predefined time frame. Publications older than 2000 were used only as background literature and were not included in the primary analysis.

Information sources
PubMed
clinicaltrials.gov
Scopus
Web of Science.

Main outcome(s) Primary outcomes include functional recovery following spinal cord injury, such as locomotor and sensory function improvement. Secondary outcomes include histological, cellular, and molecular indicators of regeneration, including lesion size, axonal regeneration, neuronal survival, angiogenesis, and expression of neurotrophic or inflammatory mediators. Clinical outcomes include neurological impairment scales, functional independence measures, quality of life assessments, and safety outcomes.

Quality assessment / Risk of bias analysis Due to the inclusion of both preclinical and clinical studies, methodological quality was assessed using study-specific considerations, including evaluation of experimental design, intervention protocols, outcome measurements, and reporting transparency. Independent reviewers screened titles, abstracts, and full texts, with disagreements resolved through discussion and consensus among reviewers.

Strategy of data synthesis Due to the considerable heterogeneity among the included studies, a quantitative meta-analysis will not be performed. The studies differ substantially in terms of study design, experimental models (in vivo and in vitro), species, spinal cord injury paradigms, and extracorporeal shock wave therapy (ESWT) treatment protocols, including variations in energy flux density, number of shocks, and timing of treatment application. Furthermore, reported outcome measures vary widely and include functional assessments, histological analyses, inflammatory markers, angiogenic factors, and other molecular outcomes, often evaluated using different methodologies and time points.

Because of these differences, direct comparability between studies is limited and pooling of data could potentially lead to misleading conclusions. Therefore, the findings will be synthesized using a structured qualitative narrative synthesis. Studies will be categorized into preclinical and clinical evidence, and preclinical studies will be further grouped according to investigated outcome domains, including functional, histological, cellular, and molecular outcomes. Results will be summarized descriptively and presented in tables to facilitate comparison across studies.The results will be synthesized using a qualitative narrative synthesis due to the expected heterogeneity of study designs, experimental models, intervention protocols, and outcome measures across the included studies. Data will be categorized into preclinical and clinical evidence. Preclinical studies will be further grouped according to investigated outcome domains, including functional, histological, cellular, and molecular outcomes. Clinical studies will be summarized based on study design, intervention protocols, patient characteristics, and reported clinical endpoints. Key findings will be presented descriptively and

summarized in tables to allow comparison between studies.

Subgroup analysis Formal quantitative subgroup analyses will not be conducted due to the methodological heterogeneity and limited number of comparable studies. However, to facilitate interpretation of the available evidence, results will be narratively stratified according to relevant study characteristics where appropriate. These may include:
• Study type (preclinical vs. clinical studies)
• Experimental model (in vivo animal models vs. in vitro/ex vivo models)
• Type of spinal cord injury (traumatic vs. ischemic injury)
• Outcome domain (functional, histological, cellular, molecular, or clinical outcomes).

This stratified descriptive approach will allow exploration of potential patterns in the reported effects of ESWT while acknowledging the heterogeneity of the available evidence.

Sensitivity analysis A formal quantitative sensitivity analysis will not be conducted due to the absence of pooled statistical analysis. However, sensitivity considerations will be addressed qualitatively by critically evaluating the influence of studies with limited methodological detail, small sample sizes, or heterogeneous experimental conditions. When interpreting the results, particular attention will be given to differences in study design, experimental models, and ESWT treatment parameters, as these factors may affect the robustness and generalizability of the findings. This approach will help ensure that the conclusions of the review are not disproportionately influenced by individual studies with methodological limitations.

Country(ies) involved Austria, Germany.

Keywords Spinal cord injury; extracorporeal shock wave therapy; shock waves; spinal cord regeneration; neuroregeneration; neurological recovery.

Contributions of each author
Author 1 - Sofie Nagele - Conceptualization, methodology, investigation, data curation, writing – original draft preparation.
Author 2 - Berit Zellmer - Conceptualization, methodology, formal analysis, investigation, writing – original draft preparation.
Author 3 - Michael Graber - Data curation, writing – review and editing.
Author 4 - Leo Winter-Pölzl - Data curation, writing – review and editing.
Author 5 - Clemens Engler - Data curation, writing – review and editing.
Author 6 - Jakob Hirsch - Data curation, writing – review and editing.
Author 7 - Sophia Schmidt - Data curation, writing – review and editing.
Author 8 - Jonas Eder - Data curation, writing – review and editing.
Author 9 - Ronja Lohmann - Data curation, writing – review and editing.
Author 10 - Maria Iannou-Nikolaidou - Data curation, writing – review and editing.
Author 11 - Vanessa Heim - Data curation, writing – review and editing.
Author 12 - Michael Grimm - Data curation, writing – review and editing.
Author 13 - Nikolaos Bonaros - Data curation, writing – review and editing.
Author 14 - Can Gollmann-Tepeköylü - Data curation, writing – review and editing.
Author 15 - Johannes Holfeld - Data curation, writing – review and editing.
Author 16 - Felix Nägele - Conceptualization, methodology, validation, supervision, project administration, funding acquisition, writing – review and editing.