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The Effects of Robotic Training on Walking and Functional Independence of People with Spinal Cord Injury: A Systematic Review, Meta-analysis and Meta-regression

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Abstract. Evidence on the effects of robotic technology is required to develop rehabilitation services. This study aimed to evaluate the effects of robot-assisted walking training on walking and functional independence in everyday life in persons with spinal cord injury (SCI) and explore the covariates associated with these effects.

We searched the MEDLINE (Ovid), CINAHL, PsycINFO, and ERIC databases until March 25, 2022. Two reviewers independently assessed the studies for inclusion. We included RCTs on people with SCI receiving robotic training. The Cochrane RoB2, meta-analysis, meta-regression, and Grading of Recommendations Assessment, Development, and Evaluation were performed.

We included 23 RCTs focusing on SCI with outcomes of walking or functional independence, of which 14 were included in the meta-analysis and meta-regression analyses. Small improvements were observed in functional independence in favor of robot-assisted walking training compared to other physical exercises (Hedges' g 0.31, 95% CI 0.02 to 0.59; $I^2 = 19.7\%$, 9 studies, 419 participants, low certainty evidence). There were no significant differences in walking ability, speed, endurance, or independence between the groups.

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Robot-assisted walking training may slightly improve functional independence, but its effects on walking ability in SCI patients is uncertain compared to other exercise. Evidence suggests little to no difference in walking independence, and the effects on walking speed and endurance are unclear. No clear evidence exists whether positive effects are linked to personal, clinical, or intervention characteristics. Robot-assisted gait training may be a viable option for improving functional independence in individuals with SCI.

Keywords: Spinal cord injuries · Robotics · Rehabilitation · Exercise · Walking · Functional status · Systematic review · Meta-analysis

1 Introduction

Every year worldwide, 250 000 to 500 000 people sustain a spinal cord injury (SCI) [1]. To reduce health care costs, robotic technology is being used more in care and rehabilitation [2] Depending on the functional ability of the injured person, walking training without robotic technology can be time consuming and requires a lot of human resources, which has promoted the development of technological innovations such as robot-assisted walking devices [3].

One of the most visible consequences of SCI is restrictions in walking function which is a major focus of rehabilitation and affects quality of life[4–6]. Walking ability consists of different aspects: walking speed, walking independence, and walking endurance [7, 8]. The combination of speed and independence is suggested as the most valid measure of improvement in gait and ambulation in individuals with SCI [7, 8]. Walking endurance is also a recommended measure to provide a comprehensive evaluation of the walking performance[7].

Recent reviews and/or meta-analyses have examined different aspects of walking, but the results have been inconclusive. No effect of robot-assisted walking interventions was found for walking speed[9–13], endurance[9, 11], or independence[10, 12] compared with other types of exercise or no intervention, while most recent reviews found significant improvements in walking endurance[10, 13], lower extremity independence[9] and mobility[13].

In addition to walking, the ability to function in everyday activities is an important goal for persons with SCI and changes in this ability are an important indication of the efficacy of rehabilitation efforts [8, 14]. There are very few published meta-analyses covering robot-assisted walking training and functional independence in persons with SCI. The most recent review found improvements in favor of robot-assisted walking training but limited the comparison to overground walking training [15]. Other, previous reviews have not found the superiority of either robot-assisted walking training or other forms of training in improving functional independence [16, 17].

A transparent rating of the certainty of the evidence has been reported only in two previous reviews [11, 16], and none have examined the association of different study factors with the effect of robot-assisted exercise. However, both are important for clinicians interpreting the results of systematic reviews and especially, when moving from evidence to recommendations. Therefore, the effects of robot-assisted walking training on different aspects of walking function and functional independence should be investigated in more detail. In addition, critical analyses of the certainty of the evidence are required.

The purpose of this systematic review and meta-analysis was to summarize randomized controlled trials (RCT) investigating the effects of robot-assisted walking training on walking and functional independence in persons with SCI because the most recent studies on the topic have been inconclusive, and therefore, high-quality updates on the current evidence are needed [9, 10, 13]. The following questions were addressed: 1) What are the effects of robot-assisted walking training on different aspects of walking ability and functional independence in adults with SCI compared to other exercises and what is the certainty of evidence? 2) Are study factors, such as personal, clinical, or intervention characteristics associated with the effects of robot-assisted walking training on walking and functional independence?

2 Methods

This systematic review and meta-analysis of RCTs was prospectively registered (PROSPERO 2022 CRD42022319235) [18] The reporting corresponds to the PRISMA and Cochrane guidelines [19, 20]. A literature search was conducted in a larger project that studied the effectiveness and meaning of robotics, virtual reality, and augmented reality in medical rehabilitation [21]. The National Library of Medicine (MEDLINE), Cumulative Index to Nursing and Allied Health Literature (CINAHL), Psychological Information Database (PsycINFO), and Education Resources Information Center (ERIC) databases were searched from inception to November 12, 2019. We conducted an updated search for studies published between August 2019 and March 25, 2022. We used MeSH or keyword terms to identify studies describing robotics and exercise combined with the Cochrane filter for RCTs. A full electronic search strategy is provided (Supplementary material). Additionally, we searched the reference lists of previously published systematic reviews.

2.1 Eligibility Criteria

We performed screening for this review in two phases. The first phase served at larger project with a wider scope[21] and included studies using the PICOS (patient, intervention, comparison, outcome, study design) framework as follows: P) adults or children requiring medical rehabilitation; I) any type of robotic device designed for rehabilitation purposes; C) conventional rehabilitation, wait-list-control, or other training modalities different from the experimental group; O) body functions and structures, activities, or participation according to International Classification of Functioning, Disability and Health (ICF), or quality of life; and S) RCT or cross-over RCT. The second phase was carried out after the updated search with more specified PICOS criteria to identify eligible studies of interest in this particular review: P) adults with both SCI and walking impairments; I) robot-assisted lower extremity or walking training intervention; C) a different type of exercise (active control) or no exercise (inactive control) or placebo as comparator; O) validated and standardized measures of walking or functional independence, and S) RCTs and cross-over RCTs. No language or publication date restrictions were imposed.

2.2 Study Selection

The titles, abstracts and full texts of the included studies were independently assessed by two researchers (AK, SH, RY, MK, OI, and EA) according to the eligibility criteria using Covidence software.[22] Disagreements were resolved by discussion or consultation with a third review team member (EA). All eligible RCTs were included in the systematic review. Meta-analyses excluded passive and other type of robot control interventions to control clinical heterogeneity.

2.3 Data Extraction and Quality Assessment

A customized template was designed in Covidence[22] to extract information on participants, interventions, outcomes, and adverse events of the included studies, and to perform quality assessment according to the Cochrane Risk of Bias 2 tool [23]. Two review team members independently extracted data and assessed the quality of the studies (AK, MK, SH, and RY). Disagreements were resolved by discussion or consultation with a third review team member (EA). Researchers of the RCTs were contacted when necessary to acquire missing data or to clarify ambiguities. If adequate data were not received despite three requests, the study or some of the outcomes of the study were excluded from the quantitative analyses. RCTs eligible for this review were included in the meta-analysis, regardless of the risk of bias judgement.

All outcomes measuring walking ability or functional independence in individuals with SCI were extracted from the included studies. A combination of the 10-m walk test (10MWT) measuring walking speed and the Walking Index for Spinal Cord Injury (WISCI), measuring walking independence or the change in the need for a walking aid, is suggested to provide the most valid measure of improvement in gait and ambulation [7, 8]. To provide the most comprehensive battery, a measure of endurance, such as the 6-min walk test (6MWT), is recommended.[7] For the walking ability meta-analysis, all walking outcomes in the included studies were prioritized in accordance[7] the following order: walking speed, walking independence, and walking endurance (Supplementary material).

Both the Spinal Cord Independence Measure (SCIM III) and the Functional Independence Measure (FIM) have been used to measure the broader functioning and independence in everyday life of individuals with SCI. The SCIM was chosen as the primary measure because it was specifically developed for persons with SCI [14, 24].

2.4 Data Analysis

To assess the treatment effect after the intervention, the meta-analysis was conducted using R software with the Metafor package for R.[25] Postintervention mean and standard deviation (SD) values were used in the analyses. Data reported as median or interquartile range (IQR) were converted to mean and SD assuming a normal distribution. A correlated effects model with robust variance estimation (RVE) using the Robumeta package on R and small-sample corrections was used, as it considers the possible dependent effect of the studies used multiple times in the same meta-analysis [26]. This was the case when a study had multiple control groups [27–29] or the study population was divided according to the level of injury [30]. It is also considered to be a more reliable analysis model for studies with small number of participants [26]. The intervention effect size (Hedges' g), 95% confidence interval (CI), and statistical heterogeneity (I2) were estimated using a forest plot. The scale of Hedges' g was evaluated as small (0.20–0.49), medium (0.50–0.79), or large (0.80 or more) effect [31]. Statistical heterogeneity was assessed as follows:0–40% might not be important heterogeneity, 30–60% may represent moderate heterogeneity, 50–90% may represent substantial heterogeneity, and 75–100% represents considerable het-erogeneity [32]. If a crossover-RCT did not have a washout period, only the first intervention period was included in the meta-analysis.

Meta-regression analysis was performed using the Metafor package for R. We computed the Univariate Mixed effects model with intercept and restricted maxi-mum-likelihood estimation to determine whether covariates related to intervention content (duration of intervention, number of training sessions per week, time of one training session, weekly total volume of training), characteristics of rehabilitees (age, time since injury in months, the baseline WISCI score), and quality of the study (domains of risk of bias) could have an impact on the results. Sensitivity analysis was conducted excluding the studies with a high risk of bias in the domains that were found to be significant in the meta-regression. The certainty of evidence was graded at the outcome level according to the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) guidelines [33–35].

3 Results

3.1 Study Selection

An initial 1 405 abstracts were identified from the electronic databases after duplicates were removed (Fig. 1). After removal of studies considered ineligible according to the PICOS criteria, 23 RCTs were included in this review and 14 in the meta-analyses with all of them studying walking ability and 9 also functional independence. The remaining studies compared two types of robot-assisted walking training [36–40], had the same patient population as another included study [41, 42], had insufficient reporting of results [43], or the comparison group included no exercise [44]. Detailed characteristics of the included studies, justification for full-text exclusions and the information requested from RCTs are provided (Supplementary material).

3.2 Study Characteristics

Participants. The walking ability meta-analysis included 498 individuals with SCI. The average time since injury ranged from 3 months to 11 years (mean 48.7 (SD 65.2) months). The functional independence meta-analysis included 419 individuals with SCI. The average time since injury ranged from 3 months to 4 years (mean 11.5 (SD 15.1) months). In both meta-analyses, the participants' average age ranged from 34 to 59 with mean 45.1 (SD 7.6) years in the walking ability meta-analysis and mean 44.0 (SD 8.6) years in the functional independence meta-analysis.

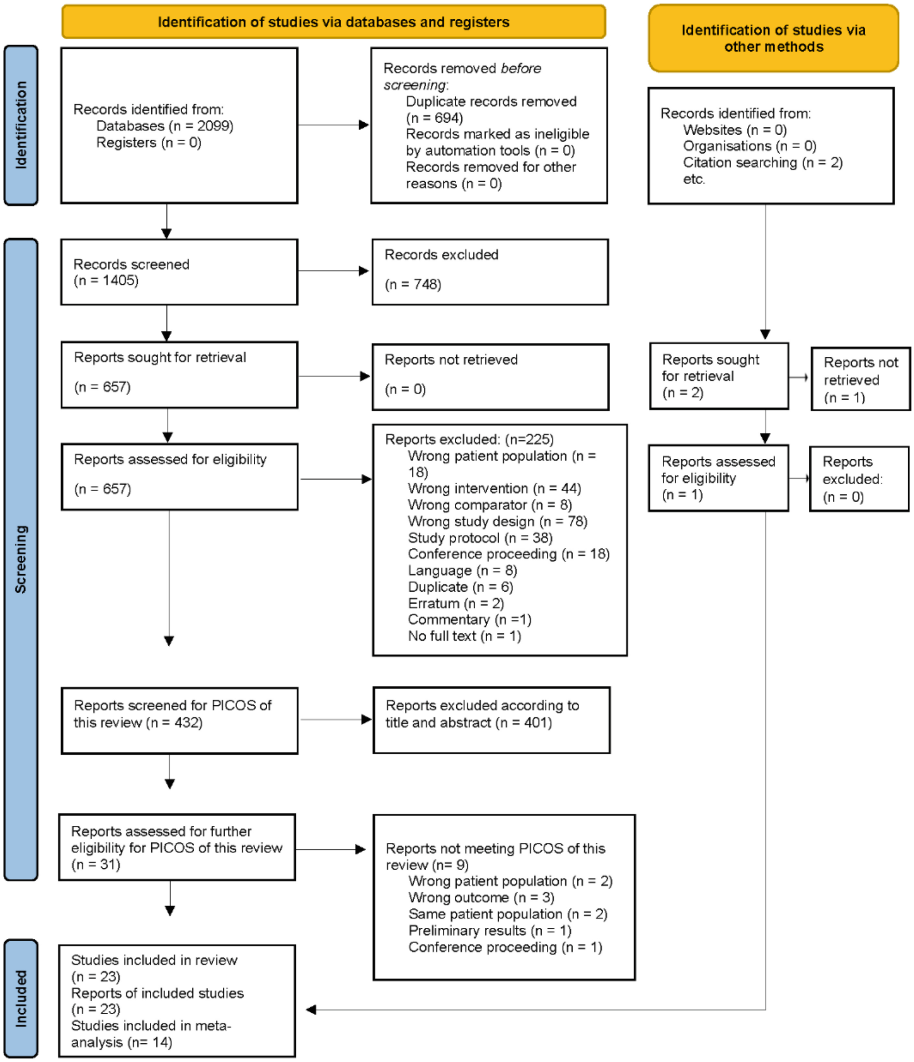

Fig. 1. Prisma flow diagram

Most commonly, the injuries of the participants in both meta-analyses were at the cervical or thoracic level, but there were also participants with lumbar-level injuries. Consequently, the meta-analyses included both paraplegic and tetraplegic participants. Most studies included participants who were grade C or D on the ASIA Impairment Scale (AIS) [45], with the majority being grade D. One study divided the participants into complete and incomplete injuries, without naming the AIS grade [46].

Robotic Interventions. In the walking ability meta-analysis, 11 studies used the exoskeleton device Lokomat (Hocoma; Zurich, Switzerland) [28–30, 46–53], 2 used the exoskeleton device Ekso (Ekso Bionics; CA, USA) [27, 54] and 1 used a 3DCaLT-robot (Shirley Ryan AbilityLab; Chicago, USA) [55]. Intervention durations varied from 3 to 24 weeks (mean 8 (SD 5)), and the duration of one session ranged from 30 to 90 min, 2 to 5 times a week. The average total training time per week was 199 min (SD 97). In the functional independence meta-analysis, all 9 studies used Lokomat. Intervention durations varied from 4 to 8 weeks (mean 7 (SD 2)), and the duration of one session ranged from 30 to 60 min, 2 to 5 times a week. The average total training time per week was 193 min (SD 107).

Body-weight support from robots in the studies in both meta-analyses was mostly utilized according to the person's needs and ranged from 0 to 78%. Less than half of the included studies reported the use of a guidance force (i.e., the assistance provided by the robotic legs to the lower extremities of the person training). The interventions took place in a hospital or university rehabilitation department. Adherence to interventions was rarely reported.

Comparisons. The comparison groups in the meta-analyses received conventional physical rehabilitation[30, 46–52, 54], with passive lower limbs mobilization [52], lower extremity strength training[53], body weight-supported treadmill training [27–29, 55] and/or overground walking training[27–30, 49, 55]. In the walking ability meta-analysis one study compared robot-assisted walking training to treadmill based or overground walking training with nerve stimulation in the control groups [28]. The amount of training in the comparison groups corresponded to that in the intervention groups in most studies.

Outcomes. Ten studies included in the meta-analysis measured walking speed, either self-selected [27, 28, 30, 49, 52–55] or not specified[29, 51], using the 10MWT or other measures, such as GAITRite-analysis. Three studies used the timed up and go (TUG) test [27, 29, 54]. Walking endurance with the 6MWT was measured in seven studies [27, 29, 30, 49, 51, 54, 55], with one study using the 2-min walk test (2MWT) [28]. Walking independence and the change in the need for a walking aid were measured using the WISCI in ten studies [27, 29, 30, 46–50, 52, 53].

The functional independence meta-analysis covered nine studies, of which four utilized the SCIM measure [48, 50, 52, 53] and five the FIM [29, 30, 46, 47, 49]. Only five studies evaluated all the subscales of SCIM [50, 52, 53] or FIM [46, 47].

3.3 Quality Assessment

The overall risk of bias was assessed as unclear [36–39, 46–48, 52, 53, 55] or high [27–30, 40–44, 49–51, 54] in each study (Supplementary material). No studies with a low overall risk of bias were found. High risk originated mainly from deviations from intended interventions but also from missing outcome data. An unclear risk of bias was found in the randomization process, deviations from the intended interventions, and selection of the reported results. Visual inspection of funnel plots suggests that some degree of publication bias is possible, smaller studies seem to favor the comparator (Supplementary material).

3.4 Synthesis of Results

Statistically significant improvements were observed in functional independence in favor of the robot-assisted walking training group compared to the control group (Hedges' g 0.31, 95% CI 0.02 to 0.59; I2 = 19.7%, 9 studies, 419 participants), whereas there were no statistically significant differences between groups in walking ability (Hedges' g 0.02, 95% CI –0.27 to 0.31; I2 = 35.5%, 14 studies, 498 participants), walking speed (Hedges' g –0.09, 95% CI –0.51 to 0.33; I2 = 32.8%, 10 studies, 290 participants), walking endurance (Hedges' g -0.03, 95% CI –0.65 to 0.58; I2 = 63.1%, 8 studies, 259 participants) or walking independence (Hedges' g 0.25, 95% CI –0.14 to 0.64; I2 = 51.3%, 9 studies, 419 participants) (Figs. 2, 3, 4, 5 and 6). Certainty of evidence proved to be low for functional independence and walking independence and very low for walking ability, speed, and endurance (Supplementary material).

In the meta-regression analyses, no relationships were found between the effects of robot-assisted walking training and intervention content or characteristics of rehabilitees. A high risk of bias in selection of the reported results was associated with the effect in functional independence. When excluding the high risk of bias study [29] from the meta-analyses, robot-assisted walking training remained statistically significant in improving functional independence compared to the control group (Hedges' g 0.35, 95% CI 0.05 to 0.64; I2 = 15.5%, 8 studies, 389 participants) (Supplementary material).

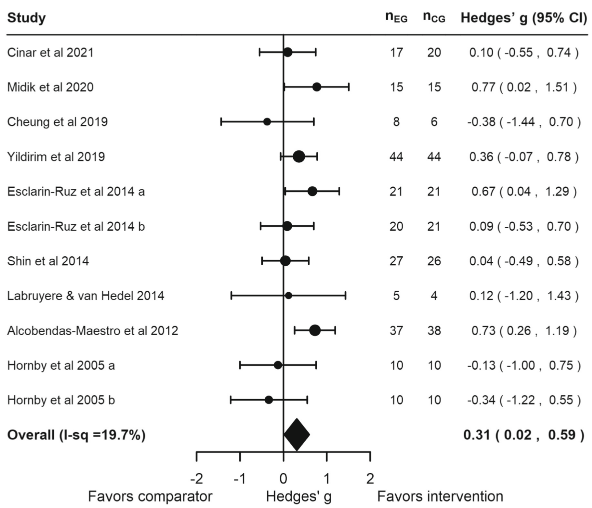

Fig. 2. Results of the meta-analysis comparing robot-assisted walking training and other physical exercise on functional independence of people with SCI.

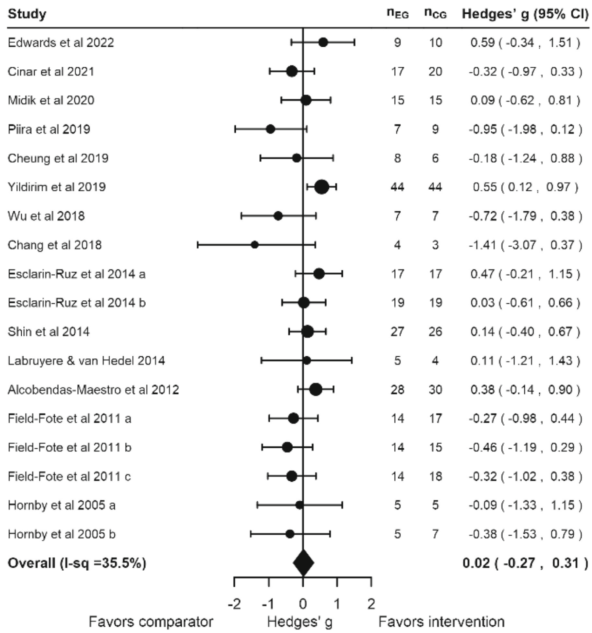

Fig. 3. Results of the meta-analysis comparing robot-assisted walking training and other physical exercise on walking ability of people with SCI.

3.5 Adverse Events

Adverse events were examined in 11 of 23 studies included. Reported adverse events were mostly mild and infrequent and four studies reported no adverse events (Supplementary material).

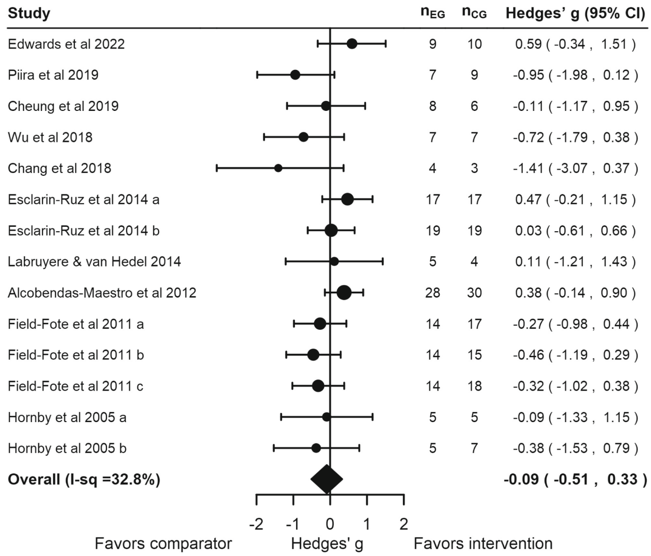

Fig. 4. Results of the meta-analysis comparing robot-assisted walking training and other physical exercise on walking speed of people with SCI.

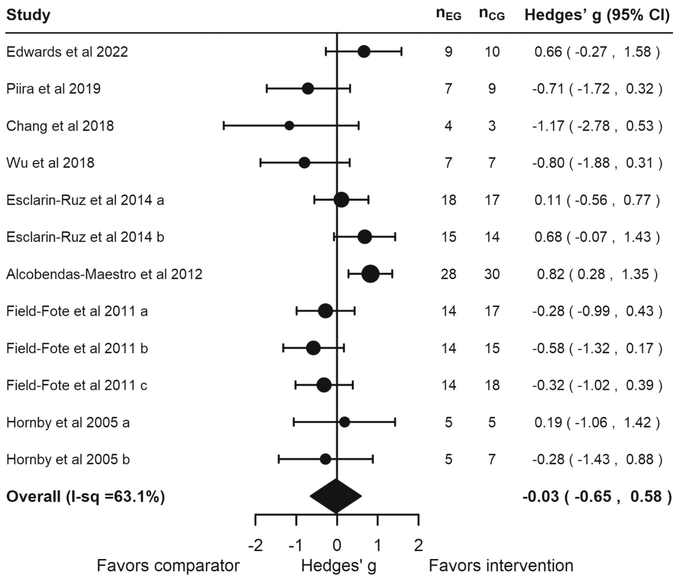

Fig. 5. Results of the meta-analysis comparing robot-assisted walking training and other physical exercise on walking endurance of people with SCI.

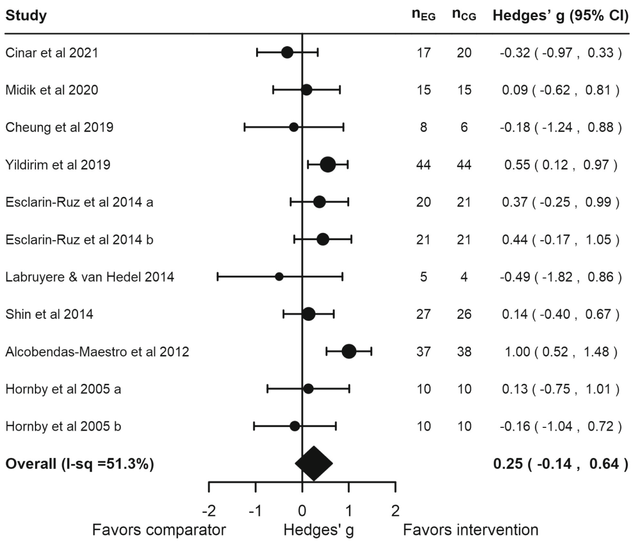

Fig. 6. Results of the meta-analysis comparing robot-assisted walking training and other physical exercise on walking independence of people with SCI.

4 Discussion

This systematic review and meta-analysis summarized evidence from the effects of robot-assisted walking training on walking and functional independence in everyday life in adults with SCI compared to those who had other physical exercises. There was a significant effect of functional independence favoring robot-assisted walking train-ing over other exercises with a small effect size (Hedges' g 0.31). No differences were found in the walking outcomes. Sensitivity analyses based on meta-regression analysis did not affect the results. The certainty of evidence was graded as low for functional independence and walking independence, and very low for walking ability, speed, and endurance. No severe adverse events were found although the reporting of RCTs regarding harms of robot-assisted training was incomplete.

The most recent systematic review of four trials by Harvey et al. [15] found significant improvements with robot-assisted walking training compared to overground walking training using SCIM and FIM. Our meta-analysis included more trials, prob-ably because of the wider scope of possible control interventions and suggests that robot-assisted walking training might be superior to other types of training in contrast to the findings of other reviews [16, 17]. Catz et al. [56] and Itzkovich et al. [57] found SCIM to be more sensitive in detecting functional ability changes than FIM and developed for patients with SCI. Therefore, including FIM in the meta-analysis may underestimate the effects of robot-assisted walking training.

Other reviews have covered various aspects of walking ability. Our review's results are mostly consistent with recent systematic reviews and meta-analyses in which robot-assisted walking interventions did not improve walking speed [9–13], endurance[9, 11] or independence [10, 12] when compared to other exercises or no intervention. Only Fang et al. [10] and Alashram et al. [13] reported significant improvements in walking endurance, and Duan et al. [9] reported significant improvements in lower-extremity independence using WISCI II. However, our meta-analyses included more studies, providing more reliable results.

To the best of our knowledge, our meta-analysis and Yang et al.'s network meta-analysis [58] are the only studies to combine multiple performance measures for walking ability outcome. Yang et al. [58] prioritized 6MWT and the Lower Extremity Motor Score (LEMS), showing significant walking improvements after robot-assisted training. This differs from our review that prioritized the 10MWT and WISCI. Previous studies suggest combining the 10MWT and WISCI to measure improvements in walking and ambulation in persons with SCI [7, 8, 59]. A measure of endurance, such as the 6MWT is also recommended [7], but varying test conditions can cause significant differences [59], hence the preference for the 10MWT and WISCI in our meta-analysis. In addition, Shin et al. [60] found that LEMS, a lower-extremity strength measure, does not significantly correlate with ambulatory function in persons with tetraplegic SCI. This finding demonstrates that different outcome measure priorities can lead to different results. More psychometric research is needed to guarantee SCI-related outcomes' sensitivity. In the future, a meta-analysis may be performed for single outcome measures if high-quality RCTs with similar outcomes are reported.

Publication bias is unlikely, as smaller studies seem to favor the comparator. However, no firm conclusions can be drawn due to the few studies and lack of larger sample sizes. The asymmetry in the funnel plots may have been caused by the high heterogeneity in the studies [61]. Our meta-analyses showed substantial statistical heterogeneity for walking endurance and moderate heterogeneity for walking independence. The meta-regression did not find clinical heterogeneity in the intervention or participant characteristics, such as time since injury, to be associated with the effect of robotic intervention. The RCTs included both paraplegic and tetraplegic individuals with SCI but did not report effects for these separately. So the level of injury could not be used as a covariate. According to Unai et al. [62] regardless of the AIS grade, paraplegic persons gain better results in the SCIM measure than tetraplegic persons; so further studies should differentiate between the two groups.

4.1 Strengths and Limitations

This study provides new information on the effects of robot-assisted walking exercise on functional independence and various aspects of walking ability in individuals with SCI. It is the first to assess the association between personal, clinical, and intervention characteristics and intervention effects. Meta-analyses excluded passive control interventions to control clinical heterogeneity. Meta-regression clarified the results, and GRADE guidelines graded the evidence certainty at the outcome level [33, 34]. To our knowledge, no recent review has provided graded clinical recommendations on this topic.

This review has limitations to consider when interpreting the results and generalizing evidence. The meta-analyses mainly included individuals with AIS grade C or D, and all but one study used an exoskeleton robot (Lokomat or Ekso), so the findings may not be generalizable. More data is needed on the effects of different robots. RCTs' methodological quality limits the reliability of the results. However, sensitivity analyses excluding studies based on the risk of bias did not alter the results. Future studies should pay particular attention to the methodological quality to ensure unbiased results.

4.2 Conclusion

Low level evidence suggests that robot-assisted walking training results in a slight improvement in functional independence, but little to no difference in walking independence in persons with SCI when compared to other exercises. The evidence is very uncertain regarding the effects of robot-assisted walking training on walking ability, walking speed, and walking endurance in persons with SCI when compared to other exercises. Heterogeneity between studies was substantial, and there is no clear evidence if positive effects were associated with age, time since injury, baseline walking independence, intervention programming, or quality of the study. Robot-assisted walking training appears to be a safe rehabilitation method for individuals with SCI. However, additional high-quality RCTs with larger sample sizes, similar outcome measures and differentiation of results between paraplegic and tetraplegic individuals are needed to further evaluate the effects and safety of robot-assisted walking training on functional independence and walking ability in individuals with SCI. When seeking to improve the functional independence of persons with SCI, robot-assisted gait training may be considered as a potential training option.

4.3 Clinical Message

Low-level evidence suggests that in people with SCI robot-assisted walking training may slightly improve functional independence but has little to no effect in walking independence compared to other exercises. Evidence is very uncertain on walking ability, speed, and endurance. Intervention or rehabilitee characteristics, and risk of bias didn't affect results.

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References

1. WHO: Spinal Cord Injury. https://www.who.int/news-room/fact-sheets/detail/spinal-cord-injury
2. EuRobotics: Strategic Research Agenda for Robotics in Europe (2014)
3. Rymer, W.Z., Burt, S., Jayaraman, A.: 13 Advanced Rehabilitation Strategies for Individuals with Traumatic Spinal Cord Injury. In: Vialle, L.R., Fehlings, M., Weidner, N. (eds.) AOSpine Masters Series, pp. 163–178. Thieme (2017)
4. Ditunno, P.L., Patrick, M., Stineman, M., Ditunno, J.F.: Who wants to walk? Preferences for recovery after SCI: a longitudinal and cross-sectional study. Spinal Cord. **46**, 500–506 (2008). https://doi.org/10.1038/sj.sc.3102172
5. Ditunno, P.L., Patrick, M., Stineman, M., Morganti, B., Townson, A.F., Ditunno, J.F.: Cross-cultural differences in preference for recovery of mobility among spinal cord injury rehabilitation professionals. Spinal Cord. **44**, 567–575 (2006). https://doi.org/10.1038/sj.sc.3101876
6. Anderson, K.D.: Targeting recovery: priorities of the spinal cord-injured population. J. Neurotrauma **21**, 1371–1383 (2004). https://doi.org/10.1089/neu.2004.21.1371
7. Anderson, K.D., et al.: Outcome measures for gait and ambulation in the spinal cord injury population. J. Spinal Cord Med. **31**(5), 487–499 (2008). https://doi.org/10.1080/10790268.2008.11753644
8. Lam, T., Noonan, V.K., Eng, J.J.: A systematic review of functional ambulation outcome measures in spinal cord injury. Spinal Cord **46**(4), 246–254 (2008). https://doi.org/10.1038/sj.sc.3102134
9. Duan, R., et al.: Clinical benefit of rehabilitation training in spinal cord injury: a systematic review and meta-analysis. Spine **46**(6), E398–E410 (2021). https://doi.org/10.1097/BRS.0000000000003789
10. Fang, C.Y., Tsai, J.L., Li, G.S., Lien, A.S.Y., Chang, Y.J.: Effects of robot-assisted gait training in individuals with spinal cord injury: a meta-analysis. Biomed. Res. Int. **2020**, 1–13 (2020). https://doi.org/10.1155/2020/2102785
11. Hornby, T.G., et al.: Clinical Practice Guideline to Improve Locomotor Function Following Chronic Stroke, Incomplete Spinal Cord Injury, and Brain Injury (2020)
12. Aguirre-Güemez, A.V., Pérez-Sanpablo, A.I., Quinzaños-Fresnedo, J., Pérez-Zavala, R., Barrera-Ortiz, A.: Walking speed is not the best outcome to evaluate the effect of robotic assisted gait training in people with motor incomplete spinal cord injury: a systematic review with meta-analysis. J. Spinal Cord Med. **42**, 142–154 (2019). https://doi.org/10.1080/10790268.2017.1390644
13. Alashram, A.R., Annino, G., Padua, E.: Robot-assisted gait training in individuals with spinal cord injury: a systematic review for the clinical effectiveness of Lokomat. J. Clin. Neurosci. **91**, 260–269 (2021). https://doi.org/10.1016/j.jocn.2021.07.019
14. Catz, A., Itzkovich, M., Agranov, E., Ring, H., Tamir, A.: SCIM – spinal cord independence measure: a new disability scale for patients with spinal cord lesions. Spinal Cord. **35**, 850–856 (1997). https://doi.org/10.1038/sj.sc.3100504
15. Harvey, L.A., Glinsky, J.V., Chu, J.: Do any physiotherapy interventions increase spinal cord independence measure or functional independence measure scores in people with spinal cord injuries? A systematic review. Spinal Cord **59**(7), 705–715 (2021). https://doi.org/10.1038/s41393-021-00638-0

16. Fisahn, C., et al.: The effectiveness and safety of exoskeletons as assistive and rehabilitation devices in the treatment of neurologic gait disorders in patients with spinal cord injury: a systematic review. Glob. Spine J. **6**(8), 822–841 (2016). https://doi.org/10.1055/s-0036-1593805
17. Wessels, M., Lucas, C., Eriks, I., De Groot, S.: Body weight-supported gait training for restoration of walking in people with an incomplete spinal cord injury: a systematic review. J. Rehabil. Med. **42**(6), 513–519 (2010). https://doi.org/10.2340/16501977-0525
18. Köyhäjoki, A., et al.: The effects of robot-assisted walking training on walking and disability of people with spinal cord injury: a systematic literature review, meta-analysis and meta-regression. https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=319235
19. Page, M.J., et al.: The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ **132**, 1–9 (2021)
20. Higgins, J., et al.: Cochrane Handbook for Systematic Reviews of Interventions version 6.3, updated February 2022. https://training.cochrane.org/handbook/current
21. Ilves, O., Korpi, H., Honkanen, S., Aartolahti, E.: Effectiveness and meanings of robots, virtual and augmented reality in rehabilitation. Systematic literature reviews. Stud. Soc. Secur. Health **159**, 1–12 (2022)
22. Covidence. https://app.covidence.org
23. Sterne, J.A.C., et al.: RoB 2: A revised tool for assessing risk of bias in randomised trials. The BMJ. **366**, 14898 (2019). https://doi.org/10.1136/bmj.l4898
24. Schuld, C., Weidner, N.: 2 Assessment of functional status and outcomes of individuals with traumatic spinal cord injury. In: Fehlings, M.J., Weidner, N., Vialle, L.R.G. (eds.) AOSpine Masters Series, pp. 11–24. Thieme (2017)
25. Viechtbauer, W.: Conducting Meta-Analyses in R with the metafor Package. J Stat Softw. **36**, 1–48 (2010). https://doi.org/10.18637/jss.v036.i03
26. Pustejovsky, J.E., Tipton, E.: Meta-analysis with Robust Variance Estimation: Expanding the Range of Working Models. Prev. Sci. **23**, 425–438 (2022). https://doi.org/10.1007/s11121-021-01246-3
27. Edwards, D.J., et al.: Walking improvement in chronic incomplete spinal cord injury with exoskeleton robotic training (WISE): a randomized controlled trial. Spinal Cord. **60**, 522–532 (2022). https://doi.org/10.1038/s41393-022-00751-8
28. Field-Fote, E.C., Roach, K.E.: Influence of a locomotor training approach on walking speed and distance in people with chronic spinal cord injury: a randomized clinical trial. Phys. Ther. **91**, 1–48 (2011). https://doi.org/10.2522/ptj.20090359
29. Hornby, T.G., Campbell, D.D., Zemon, D.H., Kahn, J.H.: Clinical and quantitative evaluation of robotic-assisted treadmill walking to retrain ambulation after spinal cord injury. Top Spinal Cord Inj. Rehabil. **11**, 1–17 (2005)
30. Esclarín-Ruz, A., et al.: A comparison of robotic walking therapy and conventional walking therapy in individuals with upper versus lower motor neuron lesions: a randomized controlled trial. Arch. Phys. Med. Rehabil. **95**, 1023–1031 (2014). https://doi.org/10.1016/j.apmr.2013.12.017
31. Cohen, J.: A power primer. Psychol. Bull. **112**, 155–159 (1992). https://doi.org/10.1037/0033-2909.112.1.155
32. Deeks, J.J., Higgins, J.P.T., Altman, D.G.: Analysing data and undertaking meta-analyses: identifying and measuring heterogeneity. In: Higgins, J.P.T., et al. (eds.) Cochrane Handbook for Systematic Reviews of Interventions, version 6.2. (2021)
33. Guyatt, G.H., Oxman, A.D., Schünemann, H.J., Tugwell, P., Knottnerus, A.: GRADE guidelines: a new series of articles. J. Clin. Epidemiol. **64**, 380–382 (2011). https://doi.org/10.1016/j.jclinepi.2010.09.011
34. Schünemann, H., Brozek, J., Gyuatt, G., Oxman, A.: GRADE Handbook. Introduction to GRADE Handbook. https://gradepro.org/resources/#handbook

35. Balshem, H., et al.: GRADE guidelines: 3. Rating the quality of evidence. J. Clin. Epidemiol. **64**, 401–406 (2011). https://doi.org/10.1016/j.jclinepi.2010.07.015
36. Benito-Penalva, J., et al.: Gait training in human spinal cord injury using electromechanical systems: effect of device type and patient characteristics. Arch. Phys. Med. Rehabil. **93**, 404–412 (2012). https://doi.org/10.1016/j.apmr.2011.08.028
37. Lam, T., Pauhl, K., Ferguson, A., Malik, R.N., Krassioukov, A., Eng, J.J.: Training with robot-applied resistance in people with motor-incomplete spinal cord injury: pilot study. J. Rehabil. Res. Dev. **52**, 113–130 (2015). https://doi.org/10.1682/JRRD.2014.03.0090
38. Wirz, M., et al.: The EMSCI network: effectiveness of automated locomotor training in patients with acute incomplete spinal cord injury: a randomized, controlled. Multicenter Trial. J Neurotrauma. **34**, 1891–1896 (2017). https://doi.org/10.1089/neu.2016.4643
39. Wu, M., et al.: Repeat exposure to leg swing perturbations during treadmill training induces long-term retention of increased step length in human SCI. Am. J. Phys. Med. Rehabil. **95**, 911–920 (2016). https://doi.org/10.1097/PHM.0000000000000517
40. Wu, M., Landry, J.M., Schmit, B.D., Hornby, T.G., Yen, S.-C.: Robotic resistance treadmill training improves locomotor function in human spinal cord injury: a pilot study. Arch. Phys. Med. Rehabil. **93**, 782–789 (2012). https://doi.org/10.1016/j.apmr.2011.12.018
41. Nooijen, C., Ter Hoeve, N., Field-Fote, E.: Gait quality is improved by locomotor training in individuals with SCI regardless of training approach. J. Neuroeng. Rehabil. **6**, 36 (2009). https://doi.org/10.1186/1743-0003-6-36
42. Kressler, J., Nash, M.S., Burns, P.A., Field-Fote, E.C.: Metabolic responses to 4 different body weight-supported locomotor training approaches in persons with incomplete spinal cord injury. Arch Phys Med Rehabil. 94, (2013). https://doi.org/10.1016/j.apmr.2013.02.018
43. Tang, Q., Huang, Q., Hu, C.: Research on design theory and compliant control for underactuated lower-extremity rehabilitation robotic systems. J. Phys. Ther. Sci. **26**, 1597–1599 (2014). https://doi.org/10.1589/jpts.26.1597
44. Duffell, L.D., Brown, G.L., Mirbagheri, M.M.: Interventions to reduce spasticity and improve function in people with chronic incomplete spinal cord injury. Neurorehabil. Neural Repair **29**, 566–576 (2015). https://doi.org/10.1177/1545968314558601
45. American Spinal Injury Association ASIA: International Standards for Neurological Classification of SCI (ISNCSCI). https://asia-spinalinjury.org/international-standards-neurological-classification-sci-isncsci-worksheet/
46. Yildirim, M.A., Öneş, K., Gökşenoğlu, G.: Early term effects of robotic assisted gait training on ambulation and functional capacity in patients with spinal cord injury. Turk. J. Med. Sci. **49**, 838–843 (2019). https://doi.org/10.3906/sag-1809-7
47. Çinar, Ç., Yildirim, M.A., Öneş, K., Gökşenoğlu, G.: Effect of robotic-assisted gait training on functional status, walking and quality of life in complete spinal cord injury. Int. J. Rehabil. Res. **44**, 262–268 (2021). https://doi.org/10.1097/MRR.0000000000000486
48. Shin, J.C., Kim, J.Y., Park, H.K., Kim, N.Y.: Effect of robotic-assisted gait training in patients with incomplete spinal cord injury. Ann. Rehabil. Med. **38**, 719 (2014). https://doi.org/10.5535/arm.2014.38.6.719
49. Alcobendas-Maestro, M., et al.: Lokomat robotic-assisted versus overground training within 3 to 6 months of incomplete spinal cord lesion. Neurorehabil. Neural Repair **26**, 1058–1063 (2012). https://doi.org/10.1177/1545968312448232
50. Mıdık, M., Paker, N., Buğdaycı, D., Mıdık, A.C.: Effects of robot-assisted gait training on lower extremity strength, functional independence, and walking function in men with incomplete traumatic spinal cord injury. Turk. J. Phys. Med. Rehabil. **66**, 54–59 (2020). https://doi.org/10.5606/tftrd.2020.3316
51. Piira, A., et al.: Robot-assisted locomotor training did not improve walking function in patients with chronic incomplete spinal cord injury: a randomized clinical trial. J. Rehabil. Med. **51**, 385–389 (2019). https://doi.org/10.2340/16501977-2547

52. Cheung, E.Y.Y., Yu, K.K.K., Kwan, R.L.C., Ng, C.K.M., Chau, R.M.W., Cheing, G.L.Y.: Effect of EMG-biofeedback robotic-assisted body weight supported treadmill training on walking ability and cardiopulmonary function on people with subacute spinal cord injuries – a randomized controlled trial. BMC Neurol. **19**, 140 (2019). https://doi.org/10.1186/s12883-019-1361-z
53. Labruyère, R., van Hedel, H.J.A.: Strength training versus robot-assisted gait training after incomplete spinal cord injury: a randomized pilot study in patients depending on walking assistance. J. Neuroeng. Rehabil. **11**, 4 (2014). https://doi.org/10.1186/1743-0003-11-4
54. Chang, S.-H., Afzal, T., Berliner, J., Francisco, G.E.: Exoskeleton-assisted gait training to improve gait in individuals with spinal cord injury: a pilot randomized study. Pilot Feasibility Stud. **4**, 62 (2018). https://doi.org/10.1186/s40814-018-0247-y
55. Wu, M., Kim, J., Wei, F.: Facilitating weight shifting during treadmill training improves walking function in humans with spinal cord injury. Am. J. Phys. Med. Rehabil. **97**, 585–592 (2018). https://doi.org/10.1097/PHM.0000000000000927
56. Catz, A., Itzkovich, M., Agranov, E., Ring, H., Tamir, A.: The spinal cord independence measure (SCIM): sensitivity to functional changes in subgroups of spinal cord lesion patients. Spinal Cord. **39**, 97–100 (2001). https://doi.org/10.1038/sj.sc.3101118
57. Itzkovich, M., et al.: The spinal cord independence measure (SCIM) version III: reliability and validity in a multi-center international study. Disabil. Rehabil. 29, 1926–1933 (2007). https://doi.org/10.1080/09638280601046302
58. Yang, F.-A., et al.: Body weight-supported gait training for patients with spinal cord injury: a network meta-analysis of randomised controlled trials. Sci. Rep. **12**, 19262 (2022). https://doi.org/10.1038/s41598-022-23873-8
59. Scivoletto, G., Tamburella, F., Laurenza, L., Foti, C., Ditunno, J.F., Molinari, M.: Validity and reliability of the 10-m walk test and the 6-min walk test in spinal cord injury patients. Spinal Cord. **49**, 736–740 (2011). https://doi.org/10.1038/sc.2010.180
60. Shin, J.C., Yoo, J.H., Jung, T.H., Goo, H.R.: Comparison of lower extremity motor score parameters for patients with motor incomplete spinal cord injury using gait parameters. Spinal Cord. **49**, 529–533 (2011). https://doi.org/10.1038/sc.2010.158
61. Sterne, J.A.C., et al.: Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials. BMJ (Online). **343**, d4002 (2011). https://doi.org/10.1136/bmj.d4002
62. Unai, K., Uemura, O., Takemura, R., Kawakami, M., Liu, M.: Association between SCIM III total scores and individual item scores to predict independence with ADLs in persons with spinal cord injury. Arch. Rehabil. Res. Clin. Transl. **1**, 100029 (2019). https://doi.org/10.1016/j.arrct.2019.100029