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REVIEW

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Effects of virtual reality rehabilitation after spinal cord injury: a systematic review and meta-analysis

Likun Wang[1], Hong Zhang[1], Haibo Ai[1] and Yuxi Liu[2,3*]

Abstract

Background Spinal cord injury (SCI) is a common neurological condition marked by damage to the spinal cord. In the field of neurological rehabilitation, virtual reality (VR) is increasingly employed for evaluating and addressing the physical limitations caused by SCI. This study aimed to describe and calculate the effect sizes of virtual reality intervention (VR) on the functional performance of SCI.

Methods We searched PubMed, Embase, Web of Science, and Cochrane Library to identify articles published before October 30, 2023, that addressed the intervention of SCI using virtual reality technology. We excluded from the meta-analysis articles that did not provide enough data to evaluate the association between virtual reality intervention and spinal cord injury. The RevMan 5.4 statistical software was used for data analysis.

Results We included 16 articles in the systematic review and pooled 9 for the meta-analysis, which were 5 randomized controlled trials (RCTs) and 4 non-RCTs, including 248 subjects. The outcome measure of the walking index for spinal cord injury, limits of stability testing and berg balance scale scores improved in non-RCTs.

Conclusion VR has shown promise in enhancing walking ability and balance function in individuals with SCI. However, the existing evidence for VR interventions in SCI patients remains limited, highlighting the necessity for future studies in this area.

Keywords Virtual reality, Spinal cord injury, Rehabilitation, Systematic review, Meta-analysis

Background

Spinal cord injury (SCI) is a common neurological disorder [1] characterized by damage to the spinal cord, which can lead to sensory, motor, bladder, and bowel dysfunction below the level of injury. The global prevalence of SCI is estimated to be 223–755 per million people. The incidence is estimated to be 10.4–83 per million people. SCI has a significant impact on society and the healthcare system [2]. SCI patients may also experience a variety of other functional impairments, such as spasticity, pain, and emotional disorders. These impairments can severely impact the patient's ability to perform daily activities and lead to a decline in quality of life [3].

*Correspondence:
Yuxi Liu
liuyuxiortho@163.com
[1]Department of Rehabilitation, The Third Hospital of Mianyang (Sichuan Mental Health Center), No. 190 Jiannan Road, Mianyang, China
[2]Department of Orthopaedics, The Affiliated Hospital of Southwest Medical University, No. 25 Taiping Street, Luzhou, China
[3]Department of Orthopaedics, The Second Hospital of Santai, No. 19 Nan Street, Luxi, Miang Yang, China

Currently, there is no specific drug for the treatment of SCI patients. The main treatment is rehabilitation training to improve the patient's function and daily living ability. Virtual reality (VR) is a rapidly developing technology that has been shown to be promising for the rehabilitation of various neurological disorders [4]. VR is a technology that creates a user-computer interface using computer software. It is immersive, constructive, and interactive. VR provides patients with multi-channel sensory input through devices such as controllers, gloves, and exoskeletons. Users can also interact with the environment [5]. This stimulation helps to promote neural functional plasticity. VR can provide a variety of safe and diverse environments, which makes it widely used in neurological disorders. Meta-analyses have shown that VR can significantly improve the upper limb function and balance function of stroke patients [6]. It can also improve the balance function of Parkinson's disease and multiple sclerosis patients to a certain extent [7]. However, the efficacy of VR intervention varies for different diseases, as each disease has different prognoses.

Although VR is also widely used in the rehabilitation of SCI patients [8], the efficacy of VR intervention is still controversial. Chang-Man An [9] et al. found that VR can significantly improve the walking index for spinal cord injury (WISCI) in SCI patients, while Michael Villiger [10] et al. found that VR intervention did not significantly improve WISCI scores in SCI patients. Amanda Vitória Lacerda de Araújo [11] et al.'s meta-analysis suggested that VR can significantly improve the motor function of SCI patients, but Amaranta De Miguel-Rubio [12] et al.'s meta-analysis found that VR training did not significantly improve upper limb motor function in SCI patients. Therefore, the efficacy of VR for SCI rehabilitation needs further exploration.

Because immersive VR training and non-immersive VR training provide different sensory stimulation to patients, they may have different effects on patient rehabilitation. However, this has not been explored in previous meta-analyses. In addition, VR for rehabilitation can be divided into commercial games and non-commercial VR programs. Commercial VR games are designed for healthy people, and patients may not be able to adapt to them well, resulting in poor rehabilitation outcomes. However, previous meta-analyses have not explored the effects of these two types of VR on SCI patients. In addition, some studies have shown that more than 8–12 weeks of exercise can significantly improve patient cardiopulmonary function [13], while 4 weeks of continuous exercise can significantly improve patient cognition, balance, and endurance [14]. However, other studies have shown that different treatment times do not have a significant difference in the improvement of patient upper limb function [15]. Therefore, the duration of VR intervention is also a worthy topic to explore. Previous meta-analyses have not studied the duration of intervention.Therefore, this meta-analysis aims to evaluate the effectiveness of VR intervention on the functional performance of SCI patients, and to explore the effects of different VR intervention times on the functional improvement of SCI patients.

Materials and methods

The approach to literature search and analysis aligned with the guidelines provided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [16]. The study was registered with the International Prospective Register of Systematic Reviews on November 19,2023 (Registration: CRD42023448409).

Search strategy and selection criteria

We searched articles published in PubMed, Embase, Web of Science and Cochrane Library from the beginning of the database to October 30, 2023 with medical subject heading (MeSH) terms and text words (or synonyms) for ("Spinal Cord Injuries" or "paraplegia") and ("Virtual Reality" or "Video Games"). Additional file 1: Table S1 details the comprehensive search strategy employed for each database.

Inclusion criteria for this meta-analysis were the following: (1) population: adults with SCI (age≥18 years); (2) intervention: any form of virtual reality intervention; (3) comparisons: we included studies comparing: VR therapy versus conventional rehabilitation interventions; VR therapy combined with conventional rehabilitation interventions versus conventional rehabilitation interventions alone; pre-post assessments of VR therapy (before and after intervention)." (4) outcome measures: any functional outcome measures related to SCI patients. The primary outcome measures encompassed motor function and balance function. Motor function was assessed through indicators such as the extremity motor score (EMS) via manual muscle strength assessment [17], the box and block test (BBT)[17], the 10-meter walk test (10WMT)[18], the WISCI [17] and timed up and go test (TUG) etc. Additionally, balance function was evaluated using measures such as the berg balance scale (BBS)[19] and limits of stability testing (LOS)[9] etc. The secondary outcome measures included evaluation of activities of daily living was conducted through instruments like the Barthel Index, measuring daily activities and overall living abilities. (5) study design: we included both randomized and nonrandomized clinical trials (including pre-post studies) published in English. Nonrandomized trials were included due to the limited number of RCT on this emerging topic of VR therapy. Analyzing the preliminary results from these studies is crucial for informing and guiding future research in this area [20]. Exclusion criteria included the following: (1) non-English literature;

(2) unable to access the full text; (3) duplicated literature. Studies with the most complete data or the latest publication date as the standard for inclusion. Additionally, the trial's acceptability and safety were assessed through the documentation of dropout rates, representing the proportion of patients withdrawing or missing follow-up for various reasons, and the recording of adverse events. Adverse events, encompassing various discomfort symptoms like nausea and vomiting, were documented, and the incidence of adverse events reflected the proportion of patients experiencing such occurrences post-intervention. These comprehensive secondary outcome measures provided a thorough evaluation of functional independence, dropout rates, and safety considerations within the study.

Literature screening

Two researchers independently conducted literature searches and screenings based on the defined search strategy and criteria. The process involved two steps: In step 1, retrieved literature from databases and relevant research reviews were imported into EndNote. Titles and abstracts of deduplicated literature were then reviewed to identify articles meeting or potentially meeting inclusion criteria. In step 2, full texts of the screened literature from step 1 were further examined based on inclusion/exclusion criteria, and reasons for exclusion were recorded. In cases of uncertainty, researchers re-evaluated full texts and, if necessary, contacted corresponding authors for clarification. Disagreements were resolved by a third researcher for a final decision.

Data extraction

Two researchers autonomously extracted data based on a predefined table, systematically reviewing and confirming the final dataset collaboratively. In case of discrepancies, resolution was achieved through discussion with a third researcher. The extracted data encompassed crucial details, including article title, country, first author's name, and publication year. Methodological particulars, such as research design, sample size, participants' demographics, SCI details, intervention specifics, and outcome measures, were meticulously included in the extraction process.

Quality assessment

Two researchers separately evaluated the quality of the included articles using an eight-item quality assessment tool (Table 1) [21–23]. The items evaluated included: adequate description of the randomization procedure; A control group; measurement of outcome measures before and after intervention; a follow-up rate of less than 70%; documentation or analysis of missing data; calculation of sample size; effective evaluation method; follow-up. The articles were rated as either "1" (the item is described or exists) or "0" (the item is described insufficiently or does

Table 1 Scoring criteria for the included studies

Scoring Criteria of Intervention Studies	
Randomization	YES: participants were randomized to study conditions at the individual, stratified, or block levels. NO: authors failed to mention randomization, specify another method of assigning group status, or group-level randomization with individual level analysis.
Control	YES: study included a comparison group—no treatment, delayed treatment, or alternate treatment. NO: study did not include a comparison group of any type.
Pre-Post	YES: behavior assessment was assessed before and after the intervention. NO: behavior assessment was administered after the intervention.
Retention	YES: study retention was at least 70% of participants who initially agreed to be in the study, as calculated by entire sample not by groups. For studies that did not report retention or dropout rates, retention can be calculated using the sample sizes used for analyses (e.g., 300 randomized, but only 250 were included in analyses, 83.3% retention). NO: study retention was less than 70% of participants who initially agreed to be in the study, as calculated by the entire sample not by groups.
Missing Data	YES: analyses were conducted with consideration for missing data that maintain fidelity of the randomization (e.g., intent to treat, imputation) or 100% retention. NO: listwise case deletion (completer analysis). Studies that failed to explicitly mention how they dealt with missing data. Authors compared the "dropped subgroup" with the selected or randomized sample but did not consider the impact of the dropped subgroup on randomization (e.g., intent to treat or imputation).
Power Analysis	YES: power analysis was conducted to determine sample size and/or effect size. NO: Neither sample size was determined by power analysis nor was effect size reported.
Validity Measure	YES: descriptions of measures included reliability and validity information, either as reference or coefficients. Measures were considered to be known, well-established measures. Objective measures were used as indications of behaviors. NO: descriptions of measures did not include reliability and validity measures. Objective behaviors were used as proxy measures.
Follow-Up	Participations were followed up.
Score	Sum of yes coded

not exist). Each "1" was worth 1 point. A study was considered to be "high quality and low risk of bias" if its score after scoring all items was above the median of 4.5 points. Studies with scores below the median were considered to be "low quality and high risk of bias".

Data analysis

We conducted a meta-analysis of all VR intervention groups from both RCTs and non-RCTs to explore the overall effect of VR intervention on functional improvement in spinal cord injury patients. Additionally, we performed a separate meta-analysis of RCTs to compare the change scores between the VR intervention and traditional rehabilitation groups. Review Manager 5.4 was used for data analysis. Cochran's Q test was used for qualitative analysis of study heterogeneity, and I^2 was used for quantitative analysis of heterogeneity. If $P>.1$, $I^2<50\%$, it suggests that there is no significant heterogeneity between studies, and a fixed-effect model is used for analysis. If $P<.1$, $I^2\geq 50\%$, it is considered that there is a large heterogeneity between studies, and a random-effect model is used for analysis. When the outcome measure is binary variable data, the combined effect size is the odds ratio (OR), and the 95% credible interval (CI). When the outcome measure being analyzed is continuous variable data, if the studies are on the same scale, the weighted mean difference (MD) and 95% CI are used; if the studies are on different scales, the standardized mean difference (SMD) and 95% CI are used. A difference is considered statistically significant if $P<.05$. Subgroup analysis and sensitivity analysis (when the number of combined items is ≥3) are also used. A funnel plot is used to evaluate the publication bias between studies.

Results

Study selection and the characteristics of included studies

As of October 30, 2023, a total of 2,588 articles were retrieved according to the search strategy, including 1,470 articles from Web of Science, 420 articles from PubMed, 193 articles from Cochrane Library, and 505 articles from Embase. Three articles were included after reviewing related reviews and references. After excluding duplicate files, 1,640 articles remained. After reading the titles and abstracts, 1,598 articles were excluded. After carefully reading 42 full texts, 25 articles were excluded (2 case reports, 4 trial designs, 6 reviews, 5 conference reports, and 9 articles that did not focus on functional outcomes). Finally, a total of 16 studies were included in the systematic review [9, 10, 24–37]. Nine of them were included in the meta-analysis [9, 10, 24–30], of which 5 were randomized controlled trials [24, 25, 27, 29, 30] and 4 were within-subject controlled studies [10, 26, 28, 33]. The detailed screening flowchart is shown in Fig. 1.

A total of 248 subjects (comparison group (CG), $n=185$; intervention group (IG), $n=63$) took part in the different studies. The highest number of participants was achieved by I.Dimbwadyo-Terrer 2016. ($n=31$). In contrast, only 5 subjects participated in the study by Tracy Wall 2015 [37]. The average age of the participants ranged from 28 to 61. Concerning the neurological level of injury, most studies included participants injured at cervical or thoracic levels. According to the American Spinal Injury Association Impairment Scale (AIS), most studies included participants with C–D levels. The main characteristics of the participants are shown in Table 2.

Regarding the intervention protocols, all the studies analyzed the effects of VR interventions through different technological devices. In terms of VR systems, the semi-immersive VR system used in 9(56%) studies, the immersive VR system used in 7(43%) studies; 6(37.5%) studies utilized commercial VR games, while 10(62.5%) studies employed specially designed VR systems. Concerning the duration and intensity of the protocols, the longest total duration of intervention was achieved by Min-Jae Lee et al. [29] with a total of 8 weeks. The longest session duration (60 min) was achieved by Lynsey D Duffell [26], N Hasnan [34], Rosanne B van Dijsseldonk [36], Tracy Wall [37], and the highest program intensity was carried out by I. Dimbwadyo-Terrer [38], Meetika Khurana [27], Min-Jae Lee [29] (five times a week). Regarding the different deficits treated, the vast majority of studies focused on the motor function and daily life abilities of SCI patients. Table 2 shows the main characteristics of the different interventions performed by the different studies.

Quality assessments

The quality of the studies ranged from 4 to 7 points (Table 3). 11(69%) studies scored higher than the median of 4.5 points and were considered to be of high quality and low risk of bias. 5(31%) studies scored lower than the median of 4.5 points and were considered to be of low quality and high risk of bias. Among the articles included in the meta-analysis, 8(89%) are considered high-quality, while 1(11%) are deemed low-quality. The most common reasons for low-quality studies were: lack of randomization, lack of a control group, lack of sample size calculation, and lack of follow-up.

Study groups included in the meta-analysis

Primary outcome

Motor function A total of 6 trials explored the effects of VR on the motor function of SCI patients, using different outcome measures, including the LEMS, BBT, 10MWT, 6-minute walk test, WISCI and TUG. For the tests mentioned in 2 or more studies, we conducted meta-analyses

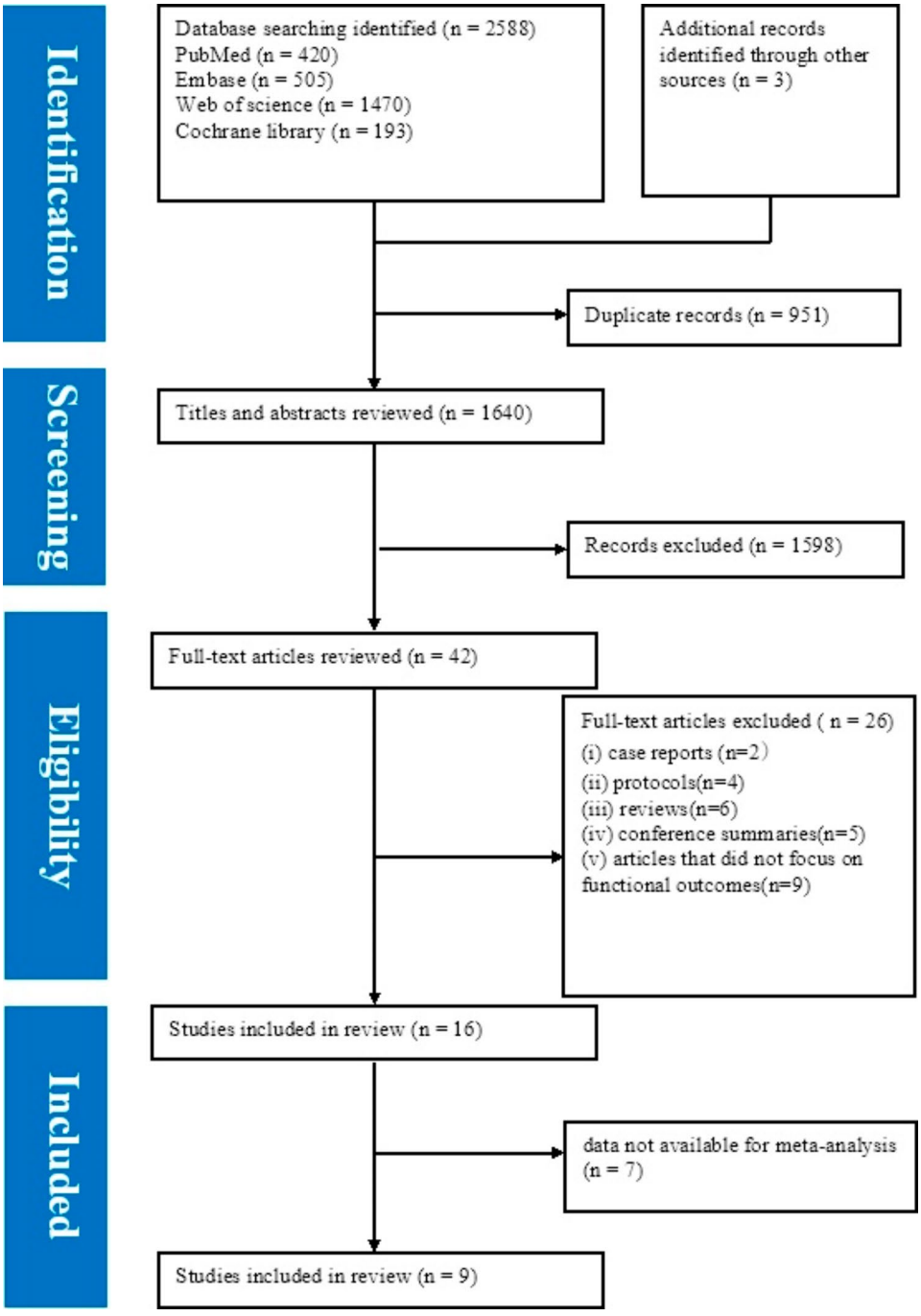

Fig. 1 flowchart

for (1) lower extremity motor score; (2) box and block test; (3) 10-meter walk test; (4) WISCI; and 5)TUG.

1) Lower extremity motor function, LEMS

A total of 2 studies [10, 28] (total of 25 participants) reported on the lower extremity motor score. The results, reported in scores, showed that there was no significant difference in the scores of patients before and after training (mean difference=2.60, 95% confidence interval: -1.58 to 6.79, P=.22) (Fig. 2). There was no significant heterogeneity (heterogeneity results: P=.96, I^2=0%), therefore a fixed-effect model was chosen.

2) Box and block test, BBT

Table 2 Characteristics of literature selected

Studies	Meta-Analysis inclusion	Country	Research type	Numbers (*n*)	Male	Female	Ages	AIS(*n*)	Level of injury	Mean time after disease onset	Interventions/Is it a commercial game	intervention time	Outcomes	Measuring instrument
Chang-Man An [9]	Yes	Korea	Prospective; cohort studies	10	6	4	44.20 ± 8.66	C(4); D(6);	C: 8 T: 2	19.20 ± 3.93(m)	Semi-immersive VR(IREX; Gesture Tek; Toronto, Canada) /No	30 min a day, 3 days a week for 6 weeks	Standing balance; Upright mobility function	LOS; BBS; TUG; WISCI II; ABC.
Da Young Lim [24]	Yes	Korea	Prospective; RCT	CG:10 IG:10 All:20	CG :8 IG:6	CG :2 IG:4	CG:61.50 ± 12.44 IG:59.00 ± 11.58	CG: C(1),D(9) IG: D(10)	CG: C(10) IG: C(10)	CG:36.50 ± 15.00(d) IG:27.90 ± 8.70(d)	CG: OT + ADL IG: OT + immersive VR (HTC VIVE VR RehabWare) /No	CG:30 min of OT + 30 min of ADL a day,4 days a week for 4 weeks IG:30 min of OT + 30 min of VR a day,4 days a week for 4 weeks	Arm and hand muscle strengths; Hand function; Independence in ADL	ASIA-UEMS; BBT; Korean version of the Spinal Cord Independence Measure; scores in the Hand Strength Test, Nine-Hole Peg Test, Action Research Arm Test.
I.Dimbwadyo-Terrer [25]	Yes	Spain	Prospective; RCT	CG :15 IG:16 All:31	CG :12 IG:10	CG :3 IG:6	CG :40.27 ± 13.61 IG:34.53 ± 13.71	CG: A(10),B(5) IG: A(11),B(5)	CG: C(15) IG: C(16)	CG:5.60 ± 2.50(m) IG:4.31 ± 2.06(m)	CG: CT IG: CT + immersive VR(Toyra) /No	CG: 1 h and 30 min per day, 5 days per week for 5 weeks IG: 30 min of VR a day, 3 days a week for 5 weeks in addition to conventional training	Motor indexes; Functional examination	Self-Care components of SCIM III; manual muscle test; The Functional Independence Measure; The Barthel Index; the UL part of Motricity Index.
Lynsey D Duffell [26]	Yes	United Kingdom	Prospective; cohort studies	11	10	1	56.54 ± 17.6	C(8);D(3)	C(3);T(7)	87.55 ± 172.31 (m)	immersive VR /Yes	1 h of VR a day, 3 days a week for 4 weeks	motor function	SCIM; WISCI; 10MWT; International Standards for Neurological Classification of spinal cord injury; Oxford scale motor power Grading; Modified Ashworth Score.
Meetika Khurana [27]	Yes	India	Prospective; RCT	CG:15 IG:15 All:30	CG:14 IG:14	CG:1 IG:1	CG:29.47 ± 7.48 IG:29.80 ± 7.32	NA	CG: T(15) IG: T(15)	CG:3.00 ± 0.66(m) IG:2.67 ± 0.72(m)	CG: PT + real-world task-specific balance training IG: PT + immersive VR(Sony PlayStation 2 and EyeToy) /No	45 min a day, 5 times a week for 4 weeks	Balance; functional performance	Self-Care components of SCIM-III; Modified Functional Reach Test; t-shirt test.
Michael Villiger [10]	Yes	Switzerland	Prospective; cohort studies	14	9	5	52.71 ± 14.85	C(2) D(12)	C(7); T(7)	5.5 ± 4.93(y)	Semi-immersive VR /No	4 weeks in 16 to 20 sessions of 45 min	lower limb function; pain	BBS; SCIM mobility; LEMS; 10MWT; NPRS.

Table 2 (continued)

Studies	Meta-Analysis inclusion	Country	Research type	Numbers (*n*)	Male	Female	Ages	AIS(*n*)	Level of injury	Mean time after disease onset	Interventions/Is it a commercial game	intervention time	Outcomes	Measuring instrument
Michael Villiger [28]	Yes	Switzerland	Prospective; cohort studies	12	NA	NA	NA	C(2) D(10)	C(6); T(5); L(1)	7.67 ± 4.78(y)	Semi-immersive VR /No	a period of 4 weeks, with 16–20 sessions of 30–45 min each	Balance; Muscle strength; Functional obility	LEMS; BBS; TUG; 10MWT; WISCI II; SCIM mobility
Min-Jae Lee [29]	Yes	Korea	Prospective; RCT	CG:10 IG:10 All:20	CG:9 IG: 4	CG:1 IG:6	CG:55.1 ± 10.41 IG: 53.7 ± 6.55	CG: C(7),D(3) IG: C(6),D(4)	CG: T(10),L(5) IG: T(11),L(4)	CG:16.5 ± 4.66(m) IG:17.4 ± 5.12(m)	immersive VR /No	CG:30 min OT + 30 min general rehabilitation a day, 5 days per week for 8 weeks IG: five 30 min OT + 30 min VR a day ,5 days per week for 8 weeks	Balance	LOS; force sensitive application.
Somya Prasad [30]	Yes	India	Prospective; RCT	CG:10 IG:12 All:22	CG:0 IG: 1	NA	CG:33.9 ± 7.1 IG: 23.7 ± 5.2	CG: A(4),B(3),C(2),D(1) IG: A(1),B(6),C(2),D(3)	CG: C(10) IG: C(12)	CG: 10.2 ± 5.7(m) IG: 10.2 ± 5.7 (m)	Semi-immersive VR (Nintendo Wii) /Yes	CG:30 min conventional therapy, 3 days a week for 4 weeks IG:30 min conventional therapy + 30 min VR(using Nintendo Wii), 3 days a week for 4 weeks	Upper limb function	BBT; The Spinal Cord Independence Measure–Self Report; Capabilities of Upper Extremity questionnaire; the World Health Organization Quality of Life-BREF.
Aarón Manzanares [31]	No	Spain	Prospective; RCT	11	7	4	42.36 ± 12.9	-	Lower than T1	-	Semi-immersive VR (Nature Trek®) /Yes	CG: 30–40 min per day, three times per week for six weeks IG: regular rehabilitation practice	quality of life	SCIM-III; Spinal cord injury quality of life questionnaire; Modified functional reach test.
Madhusree Sengupta [32]	No	India	Prospective Comparative Pre-Post Study	21	17	4	28 ± 12.1	A(6),B(5),C(5),D(5)	-	< 6 (m)	CG: conventional exercise therapy IG: conventional exercise therapy + semi-immersive VR /No	CG: conventional exercise therapy IG: 30 min semi-immersive VR therapy, 5 days a week for 3 weeks	Balance	BBS; balance section of the Tinetti Performance-Oriented Mobility Assessment; Functional Reach Score.
Michael Villiger [33]	No	Switzerland	a longitudinal pilot study	9	5	4	55.1 ± 15.8	-	-	-	semi-immersive VR /Yes	45 min semi-immersive VR therapy, 4–5 days a week for 4 weeks	Upper limb function	LEMS; BBS; WISCI II.

Table 2 (continued)

Studies	Meta-Analysis inclusion	Country	Research type	Numbers (*n*)	Male	Female	Ages	AIS(*n*)	Level of injury	Mean time after disease onset	Interventions/Is it a commercial game	intervention time	Outcomes	Measuring instrument
N Hasnan [34]	No	Australia	a longitudinal, prospective before–after trial.	8	-	-	-	-	-	-	semi-immersive VR /Yes	60 min semi-immersive VR therapy, 3 days a week for 4 weeks	Motor function	Arm +leg peak power.
Meyke Roosink [35]	No	Canada	a longitudinal, prospective before–after trial.	9	7	2	53 ± 13	-	Lower than C4	> 3 (m)	immersive VR /NO	The experiment consisted of two sessions (1.5 h each, at least 1 week apart to avoid carry-over effects) of interactive virtual walking.	Pain /emotion/motor	LEMS; BBS; TUG; SCIM; WISCI II; and 10MWT and 6 min walking tests.
Rosanne B van Dijsseldonk [36]	No	Netherlands	a longitudinal, prospective before–after trial.	15	11	4	59 ± 12	-	-	> 6 (m)	immersive VR /NO	12 1-h training sessions spread over a 6-week period.	Balance	the 2 min walking test.
Tracy Wall [37]	No	America	a longitudinal, prospective before–after trial.	5	5	0	58.6	-	-	> 12 (m)	semi-immersive VR /Yes	60 min semi-immersive VR therapy, 2 days a week for 7 weeks	Motor function	TUG; forward functional reach test and lateral functional reach test; RAND 36-Item Short Form Health Survey.

ABC: Activities-Specific Balance Confidence Scale; AIS: American Spinal Injury Association Impairment Scale; BBS: Berg Balance Scale; BBT: Box and Block Test; CG: Control Group; d: Day; IG: Intervention Group; LEMS: Lower Extremity Motor Score; LOS: Limit of Stability; m: Month; min: Minute; OT: Occupational Therapy; PHQ-8: Patient Health Questionnaire-8; RCT: Randomised Controlled Trial; SCIM: Spinal Cord Independence Measure; TUG: Timed Up and Go; UEMS: Upper Extremity Motor Score; WISCI: Walking Index for Spinal Cord Injury; 10MWT: 10 m Walking Test; y: Year

Table 3 Assessment of literature quality

Studies	Randomization	Control	Pre-Post	Retention	Missing data	Power analysis	Validity measure	Follow-Up	Score	Inclusion in meta-analysis
Chang-Man An [9]	0	0	1	1	1	0	1	0	4	Yes
Da Young Lim [24]	1	1	1	1	1	0	1	0	6	Yes
I. Dimbwadyo-Terrer [38]	1	1	1	1	1	0	1	1	7	Yes
Lynsey D Duffell [26]	0	0	1	1	1	0	1	1	5	Yes
Meetika Khurana [27]	1	1	1	1	1	0	1	0	6	Yes
Michael Villiger [10]	0	0	1	1	1	0	1	1	5	Yes
Michael Villiger [28]	0	0	1	1	1	0	1	1	5	Yes
Min-Jae Lee [29]	1	1	1	1	1	1	1	0	7	Yes
Somya Prasad [30]	1	1	1	1	1	0	1	0	6	Yes
Aarón Manzanares [31]	1	1	1	1	1	0	1	0	6	No
Madhusree Sengupta [32]	0	0	1	1	1	1	1	0	5	No
Michael Villiger [33]	0	0	1	1	1	0	1	1	5	No
N Hasnan [34]	0	0	1	1	1	0	1	0	4	No
Meyke Roosink [35]	0	0	1	1	1	0	1	0	4	No
Rosanne B van Dijsseldonk [36]	0	0	1	1	1	0	1	0	4	No
Tracy Wall [37]	0	0	1	1	1	0	1	0	4	No

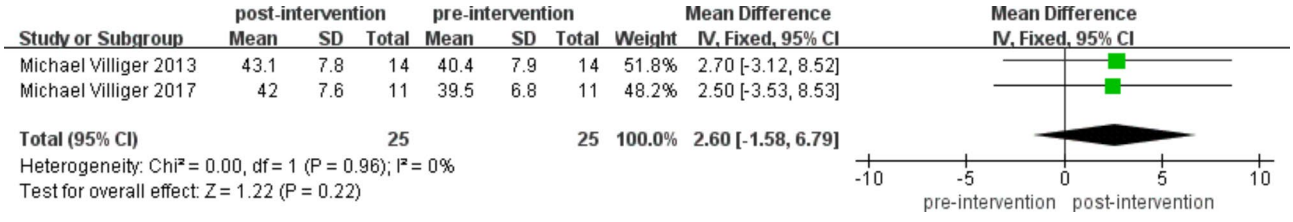

Fig. 2 Comparison before and after VR training: forest plot of EMS

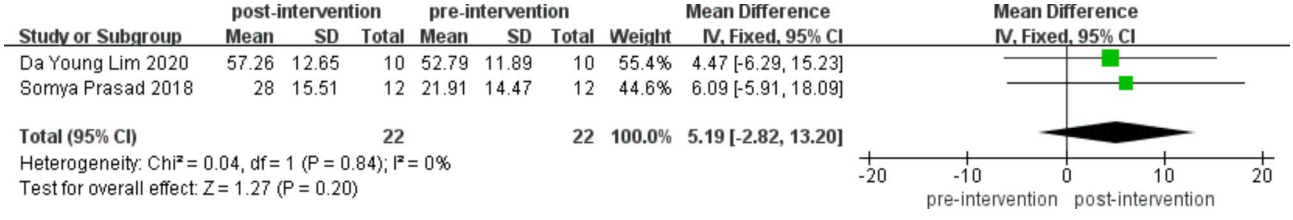

Fig. 3 Comparison before and after VR training: forest plot of BBT

A total of 2 studies [24, 30] (total of 22 participants) reported on the box and block test score. The results, reported in scores, showed that there was no significant difference in the scores of patients after and before training (mean difference=5.19, 95% confidence interval: -2.82 to 13.20, P=.20) (Fig. 3). The meta-analysis revealed that the VR group showed significantly greater improvements compared to the traditional rehabilitation training group, as indicated by the change scores from pre- to post-intervention (mean difference=4.37, 95% confidence interval:

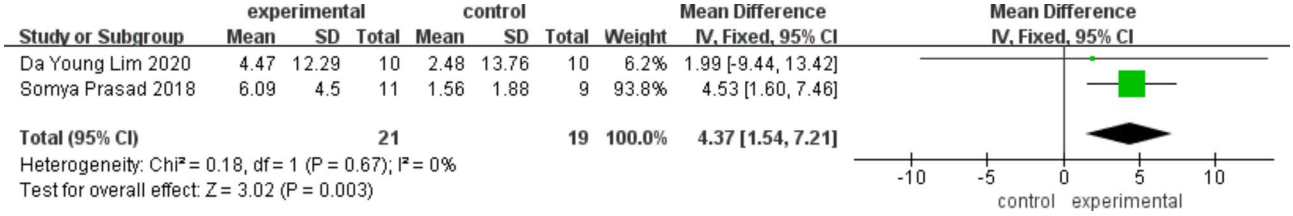

Fig. 4 Comparison of change scores between VR group and traditional group: forest plot of BBT

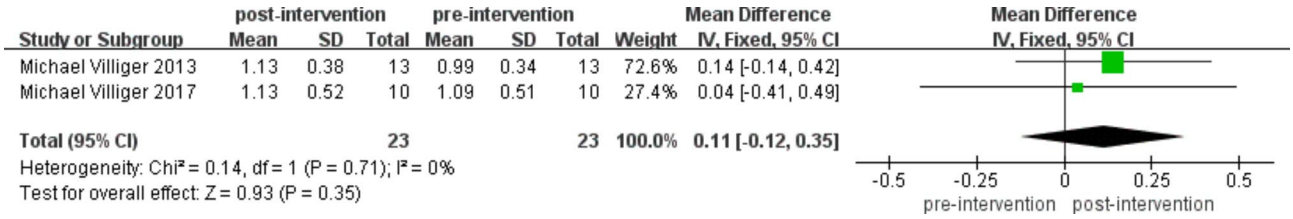

Fig. 5 Comparison before and after VR training: forest plot of 10WMT

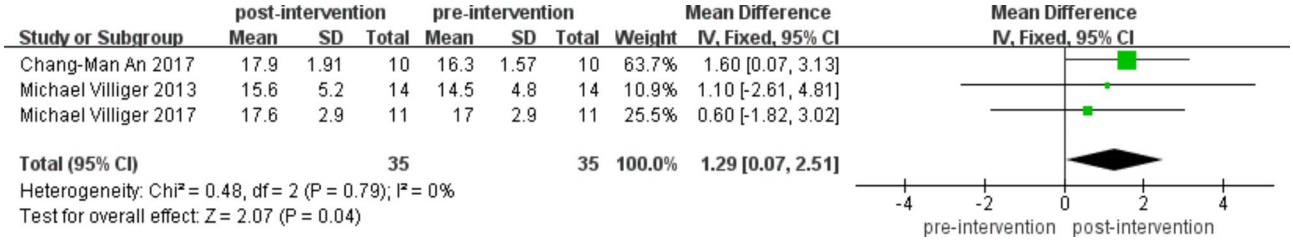

Fig. 6 Comparison before and after VR training: forest plot of WISCI

1.54 to 7.21, P=.003) (Fig. 4). Both results showed no significant heterogeneity (heterogeneity results: P=.84, I^2=0%; P=.67, I^2=0%). Therefore, a fixed-effect model was chosen for both results.

3) 10 M walk test, 10WMT

Two studies [10, 28] (total of 23 participants) reported on the 10-meter walk test for patients before and after training. The results showed that there was no significant difference in the 10-meter walk test speed (meters per second) before and after training (mean difference=0.11, 95% confidence interval: -0.12 to 0.35, P=.35) (Fig. 5). The study results showed no significant heterogeneity (heterogeneity results: P=.71, I^2=0%), therefore a fixed-effect model was chosen.

4) Walking index for spinal cord injury, WISCI

Three studies [9, 10, 28] (total of 35 participants) reported on the WISCI score. The results, reported in scores, showed that there was a significant difference in the WISCI score before and after training (mean difference=1.29, 95% confidence interval: 0.07 to 2.51, P=.04) (Fig. 6). The study results showed no significant heterogeneity (heterogeneity results: P=.79, I^2=0%), therefore a fixed-effect model was chosen.

5) Timed up and go test, TUG

Two studies [9, 28] (total of 20 participants) reported on the "stand-up-walk" timing test score. The results showed that there was no significant difference in the scores (seconds) of patients before and after training (mean difference=1.98, 95% confidence interval: -0.72 to4.69, P=.15) (Fig. 7). The study results showed no significant heterogeneity (heterogeneity results: P=.73, I^2=0%), therefore a fixed-effect model was chosen.

Balance function Three studies evaluated the effects of VR on the balance function of SCI patients, including the LOS, and the BBS. A meta-analysis was conducted on these studies.

1) Limits of stability testing, LOS

Two studies [9, 29] (total of 20 participants) reported on the stability limit test. The results, reported in scores, showed that there was a significant difference in the stability limit test scores before and after training

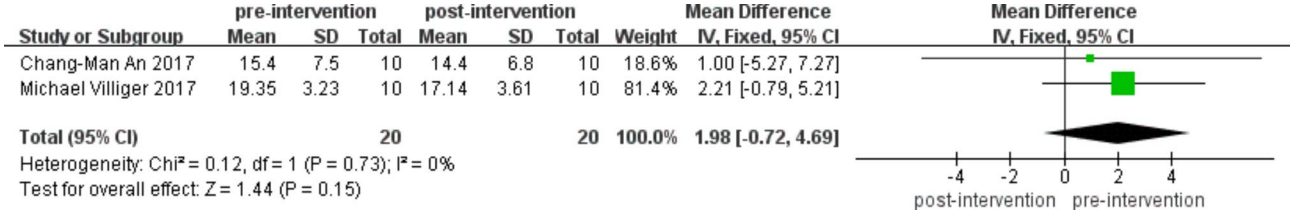

Fig. 7 Comparison before and after VR training: forest plot of TUG

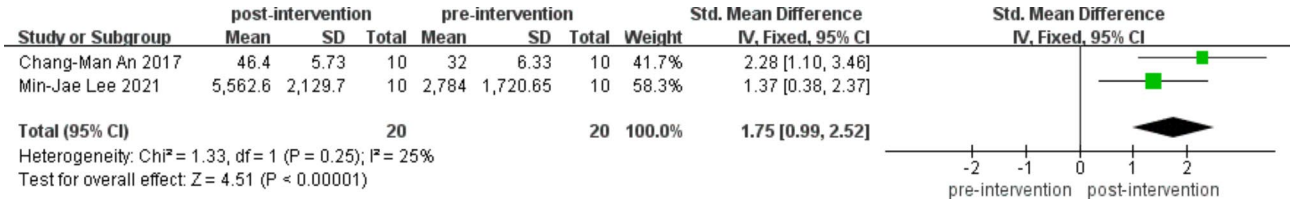

Fig. 8 Comparison before and after VR training: forest plot of LOS

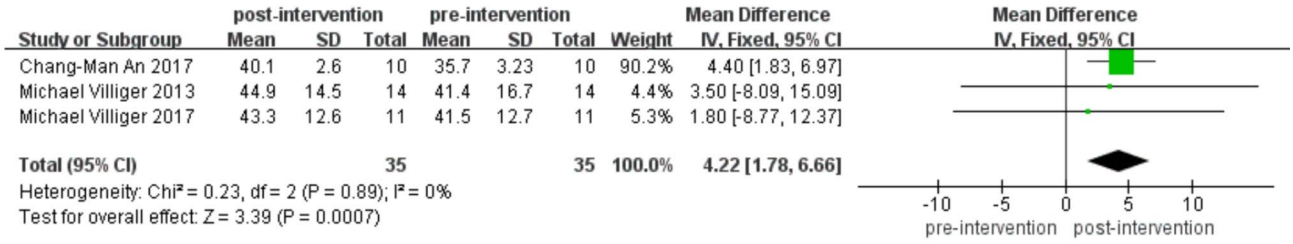

Fig. 9 Comparison before and after VR training: forest plot of BBS

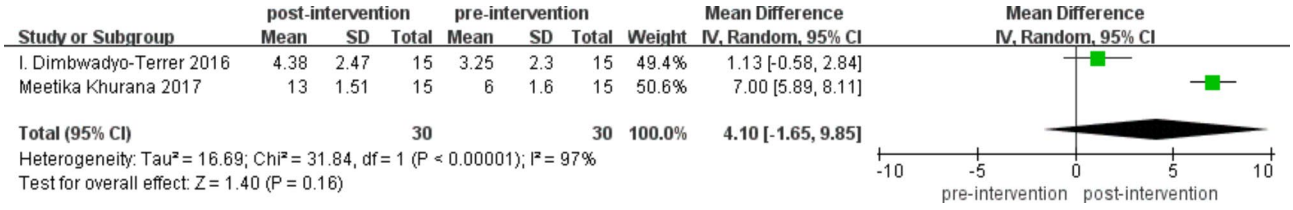

Fig. 10 Comparison before and after VR training: forest plot of SCIM self-care

(standardized mean difference=1.75, 95% confidence interval: 0.99 to 2.52, $P<.01$) (Fig. 8). The study results showed no significant heterogeneity (heterogeneity results: $P=.25$, $I^2=25\%$), therefore a fixed-effect model was chosen.

2) Berg balance scale, BBS

Three studies [9, 10, 28] (total of 35 participants) reported on the Berg Balance Scale score. The results, reported in scores, showed that there was a significant difference in the Berg Balance Scale scores before and after training (mean difference=4.22, 95% confidence interval: 1.78 to 6.66, $P<.01$) (Fig. 9). The study results showed no significant heterogeneity (heterogeneity results: $P=.89$, $I^2=0\%$), therefore a fixed-effect model was chosen.

Secondary outcome measures

Activities of daily living Spinal cord independence measure, SCIM

Six studies [10, 24–28] (total of 80 participants) reported on the spinal cord independence measure (SCIM) score[17]. Meta-analyses were conducted separately for SCIM self-care, SCIM mobility, and total SCIM scores. The results, reported in scores, showed that there was no significant difference in the scores of patients before and after training (SCIM self-care: mean difference=4.10, 95% confidence interval: -1.65 to 9.85, $P=.16$; SCIM mobility: mean difference=1.80, 95% confidence interval: -2.25 to 5.85, $P=.38$;total SCIM scores: mean difference=2.69, 95% confidence interval: -8.27 to 13.65, $P=.63$) (Figs. 10, 11 and 12). There was also no significant difference between the VR group and the traditional

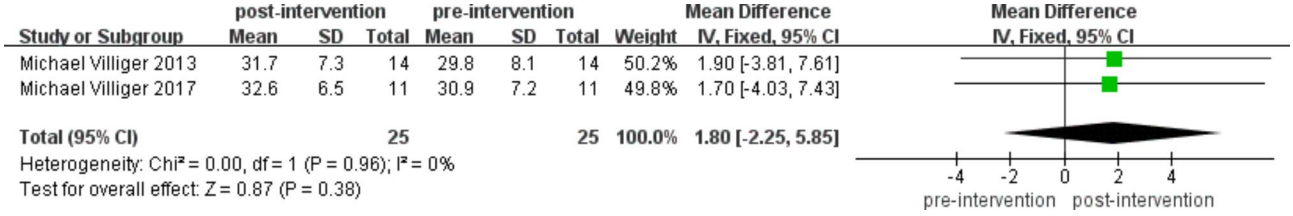

Fig. 11 Comparison before and after VR training: forest plot of SCIM mobility

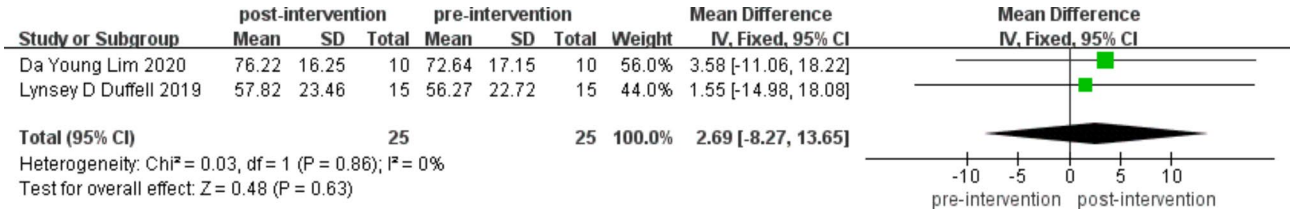

Fig. 12 Comparison before and after VR training: forest plot of total SCIM scores

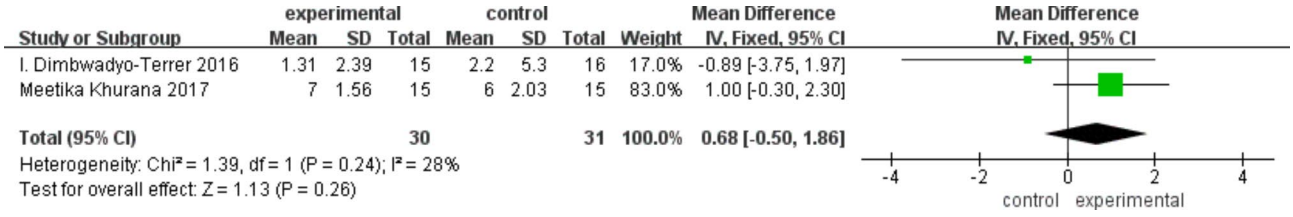

Fig. 13 Comparison of change scores between VR group and traditional group: forest plot of SCIM Self-Care

Table 4 Subgroup Analysis results

	Studies	Comparison statistics				Heterogeneity	*P*-value be-tween sub-groups
		MD	SMD	95% CI	*P*-value	I^2(%)	
Subgroup analysis of walking index for spinal cord injury							
single intervention time <45 min VS ≥ 45 min							
single intervention time <45 min	2	1.31	/	-0.02, 2.61	0.05	0	0.91
single intervention time ≥ 45 min	1	1.10	/	-2.61,4.81	0.56	/	

Abbreviations: CI, confidence interval; df, degrees of freedom; SMD, standardized mean difference, [a]P values are significantly different

rehabilitation training group in terms of the change scores from pre- to post-intervention (MD=0.68, 95% confidence interval: -0.50 to 1.86, *P*=.26) (Fig. 13). All results showed no significant heterogeneity (SCIM self-care: *P*=.24, I^2=28%; SCIM mobility: *P*=.96, I^2=0%; total SCIM scores: *P*=.86, I^2=0%), so the fixed-effect model was chosen.

Dropout rate Ten studies reported on dropout rates for the trials. Three studies [26, 29, 30] with a total of five patients withdrew from the trial, with a dropout rate of 2.02%. One patient [29] withdrew from the trial before randomization due to sudden deterioration of the disease. Three patients [26, 30] withdrew from the trial after receiving VR training, and one patient [30] withdrew from the traditional rehabilitation group after baseline assessment. The dropout rates for the VR training group and the traditional rehabilitation group were 4.76% and 0.54%, respectively.

Adverse event The study by Lynsey D Duffell et al. [26] reported no adverse events during the trial. The remaining studies did not report the number and type of adverse events.

Subgroup analysis

Subgroup analyses were performed for the WISCI (Table 4). The results of the subgroup analysis indicate that regardless of whether the single intervention time is less than 45 min (MD=1.31, 95% confidence interval: -0.02 to 2.61, *P*=.05) or 45 min or more(MD=1.10, 95% confidence interval: -2.61 to 4.81, *P*=.56), there was no significant improvement in the WISCI scores of SCI

patients before and after VR training. The forest plot is located in Additional file 2: Figs. S1.

Sensitivity analysis

When the number of studies included in the meta-analyses was equal to or greater than 3, we performed sensitivity analysis to explore the stability of the results. In the sensitivity analysis, we performed a leave-one-out analysis where each study was omitted one at a time, and the remaining studies were re-analyzed to determine if the overall meta-analysis results changed significantly with the exclusion of each individual study. Table 5 displays the estimates of effect sizes and their corresponding confidence intervals for each iteration of the analysis, showing how the removal of each specific study impacts the overall meta-analysis results. This method helps to assess the robustness of the overall findings and identify if any single study disproportionately influences the meta-analysis results. The results for both the SCI walking index (WISCI) and the Berg Balance Scale (BBS) changed when Chang-Man An [9] was removed.

Publication bias

The funnel plots for the LEMS, BBT, 10WMT, WISCI, LOS, TUG, BBS, SCIM self-care, SCIM mobility, total SCIM scores and SCIM self-care (randomized controlled trial) were generally symmetrical, indicating no obvious publication bias. The funnel plots for the motor function score and spinal cord independence measure (within-subject trial) were asymmetrical, indicating publication bias. The results are presented in Additional file 3: Figs. S2.

Trials not included in meta-analysis

Among the seven studies excluded from the meta-analysis, one was an RCT, while the remaining six were non-RCTstudies. The studies were excluded from the meta-analysis either due to missing data or because the scales used in these studies were only employed in single studies, preventing a meta-analysis. Aarón Manzanares [31] conducted a study where 11 participants were randomly assigned to either an experimental group or a control group. In addition to conventional rehabilitation treatment, the experimental group received a semi-immersive VR training for 30–40 min per day, three times per week for six weeks. The results indicated that the experimental group showed significant improvements in mobility, balance variables, and overall quality of life. Sengupta M's study [32] indicated that there was a significant improvement in balance ability for SCI patients before and after VR training. However, Rosanne B van Dijsseldonk's research [36] showed that there was no significant improvement in balance ability for SCI patients after VR training. Michael Villiger found that VR can improve functional outcomes in SCI patients by enhancing structural brain plasticity at the cortical and brainstem levels following training [33]. Additionally, Hasnan N [34] found that peak aerobic fitness in patients significantly improves before and after VR training.

Table 5 Sensitivity analysis

Study omitted	Estimate	Lower CI limit	Upper CI limit
Walking index for spinal cord injury, WISCI			
Chang-Man An [9]	0.75	-1.28	2.78
Michael Villiger [10]	1.31	0.02	2.61
Michael Villiger [28]	1.53	0.11	2.94
Berg balance scale, BBS			
Chang-Man An [9]	2.57	-5.24	10.38
Michael Villiger [10]	4.25	1.76	6.75
Michael Villiger [28]	4.36	1.85	6.87

Discussion

While previous meta-analyses on VR in SCI exist, this meta-analysis is particularly valuable and unique in its focus on evaluating functional outcomes. We analyzed the rehabilitation effects of VR in SCI patients, including motor function, balance function, independent living ability, and the occurrence of adverse events. These studies were conducted in different countries, including Korea, the United States, Spain, India, Canada and Netherlands. Different VR systems were used, including Toyra, Sony PlayStation 2, HTC VIVE VR Rehab Ware, and Samsung Galaxy S3. The results showed that VR training significantly improved walking ability and balance function in SCI patients. Since only one study reported adverse events, the safety of VR interventions cannot be effectively assessed. More studies are needed to properly evaluate VR's safety in rehabilitation. However, compared to traditional rehabilitation training, the dropout rate for VR is higher. This indicates that participants may be less likely to stick with VR rehabilitation compared to traditional methods. This could be due to issues with VR equipment or software that may cause frustration, or because some patients experience dizziness or discomfort after VR training [39].

Rehabilitation effects of virtual reality training on motor function in SCI patients

Our investigation demonstrates that VR interventions have the potential to enhance WISCI among individuals with SCI. The WISCI is a reliable metric for evaluating patients' walking ability, a fundamental aspect of mobility rehabilitation [40]. This index assesses essential components of walking, such as lower limb strength, balance, and coordination, which are critical for activities like turning, transferring, standing, and walking. While our overall analysis shows a significant improvement in WISCI scores following VR training, the subgroup

analysis based on single intervention time (<45 min and ≥45 min) revealed no significant effect of VR on WISCI improvement in either subgroup. This suggests that the significant improvement in WISCI observed in the overall analysis may not be directly tied to the length of individual VR sessions. It is possible that factors other than the length of a single intervention session, such as the cumulative intervention time or the type of VR tasks used, play a more crucial role in enhancing walking ability. Therefore, while VR has demonstrated a potential benefit in improving walking function, these improvements may not be solely dependent on the duration of each session, highlighting the need for further research to optimize VR intervention protocols for SCI patients. Notably, our findings reveal a significant improvement in these areas, following VR training among SCI patients. However, our study also indicates that there was no significant improvement in TUG performance after VR training. This may be because the TUG test focuses more on evaluating overall dynamic balance, walking speed, and turning ability—skills that require a higher level of walking competence [41]. Compared to the WISCI, the TUG test is simpler, with more coarse-grained scoring criteria. Achieving significant improvements in these areas may necessitate a longer duration or higher intensity of training, which the current VR intervention may not adequately provide. Therefore, further research is needed to explore the effects of VR on walking ability in greater detail.

Our comprehensive meta-analysis reveals that VR interventions do not significant improvements in lower extremity motor function (LEMS) in SCI patients. Motor function restoration stands as a pivotal rehabilitation objective for SCI patients. Despite VR's inherent advantages in rehabilitation, such as heightened patient engagement, motivational reinforcement, and enhanced training precision [42], previous meta-analyses [12, 42] alongside our own findings suggest a limited impact on motor function improvement. In particular, the meta-analysis conducted by Amaranta De Miguel-Rubio et al. [42] underscores this observation, attributing the underwhelming outcomes of VR to the specific VR equipment utilized. Notably, the studies included in the meta-analysis for the LEMS outcome all employed non-immersive VR platforms, whereas immersive VR technologies have been shown to enhance patient focus. Consequently, immersive VR modalities may hold promise in augmenting lower extremity motor function among SCI patients, whereas non-immersive approaches may fall short in this regard [43]. Moreover, various other factors inherent to exercise training may influence rehabilitation efficacy, such as the nature of tasks within each VR program and individual participant characteristics. Hence, a more nuanced analysis is warranted to identify an optimal VR framework tailored to the specific motor function rehabilitation needs of SCI patients.

Our study findings revealed that although there was no significant overall improvement in BBT scores for SCI patients before and after VR training, the VR group showed significant improvement compared to the traditional rehabilitation group. The International Classification of Functioning, Disability and Health (ICF) [44] posits that activity limitations may be influenced by functional level and structural damage, suggesting that impaired upper extremity motor function could also compromise hand function. For instance, in the BBT test, lifting a block and moving it to a box requires coordinated movements of the arm and hand, where VR training may show greater effectiveness in improving such coordination tasks. Another possible explanation is that the content of VR training may be more targeted than traditional rehabilitation, particularly in terms of fine motor skills and upper limb coordination. However, while the VR group demonstrated relatively greater improvement, the training may still not be fully optimized to maximize hand function gains. Therefore, future research should explore how different types of VR software or training content affect hand function in SCI patients to better understand VR's potential advantages.

Rehabilitation effects of virtual reality training on balance function in SCI patients

Our analysis demonstrated a significant enhancement in the balance function of SCI patients following VR interventions. Although most patients prioritize walking ability as the ultimate rehabilitation goal post-spinal cord injury [9], it is imperative to recognize the crucial role of balance function in facilitating walking. Both Limits of Stability (LOS) and Berg Balance Scale (BBS) tests serve as reliable measures of patients' balance function. LOS evaluates balance under relatively fixed center of gravity conditions, whereas BBS assesses balance under constantly shifting center of gravity conditions [45]. Our study observed significant improvements in both LOS and BBS scores post-VR training, corroborating findings from Chang-Man An's experiment [9]. In their study, participants engaged in various torso movements and tasks within a virtual environment, promoting self-disturbed balance and enhancing standing balance. Nonetheless, it is noteworthy that while frontal plane balance function notably improved, sagittal plane balance ability did not exhibit significant improvement, possibly due to variations in exercise directions during the specific training regimen. Additionally, Kim's [45] findings further underscored VR's significant impact on enhancing BBS scores, highlighting VR's potential in improving the balance function of SCI patients.

Rehabilitation effects of virtual reality training on daily living skills in SCI patients

Our analysis indicates that VR interventions did not result in significant improvements in SCIM self-care, SCIM mobility, or total SCIM scores. The primary aim of rehabilitation for SCI patients is to enhance their daily living abilities. SCIM, a disability scale tailored for SCI patients, proves to be highly sensitive to functional changes during rehabilitation, making it a crucial assessment tool [46]. Therefore, it's imperative to initiate daily living ability training promptly once the patient's condition stabilizes. Achieving improvements in daily living abilities necessitates progressive and prolonged rehabilitation training, with individual intervention sessions requiring extended durations. Presently, VR training programs predominantly focus on specific functionalities, with limited offerings for daily living ability training. Hence, there's a need to develop VR scenarios tailored to the daily life activities of patients. This approach would enable us to provide targeted rehabilitation training to enhance the daily living skills of SCI patients in the future.

Acceptance and adverse events of virtual reality training in patients with SCI

The findings of this study indicate that SCI patients exhibit a lower acceptance rate of VR compared to traditional training methods. Virtual reality (VR) interventions may elicit adverse reactions in patients, such as dizziness and headaches. However, among the studies included in our analysis, only Lynsey D Duffell et al.'s [26] study reported no adverse events during the trial. The remaining studies did not provide information on whether patients experienced adverse events. Previous research has suggested that VR is generally safe and has a low incidence of adverse reactions [28]. However, adverse reactions are rarely mentioned in current studies focusing on VR rehabilitation for SCI patients. Hence, future investigations should prioritize assessing the frequency and nature of adverse events experienced by patients.

Limitations of the study

This study has several limitations. Firstly, the inclusion of a limited number of trials, mostly non-randomized controlled trials, restricts the robustness of our conclusions. Only 5 studies are RCTs, and most meta-analyses include only two studies. Additionally, among the included RCTs, most compare traditional rehabilitation training with VR, which only indicates the relative merits of VR training compared to traditional training. Alternatively, if VR training is added as an extra, it does not rigorously demonstrate the advantages of VR training, as it may merely reflect the results of additional training. Therefore, future research needs more RCTs comparing VR interventions with VR placebo or comparing VR interventions with interventions of similar content in the real world to further explore the advantages and disadvantages of VR training itself. Secondly, the diverse VR training methods across studies hinder the assessment of different VR software effects on SCI patient rehabilitation. Moreover, we didn't conduct subgroup analysis based on injury severity. Additionally, the impact of the intensity or total hours of VR training on outcomes remains unclear due to the limited number of studies. More research is needed to investigate how different training intensities and durations affect rehabilitation results, as these factors are crucial for optimizing VR intervention protocols. Lastly, instability in some outcome measures and potential publication bias in others suggest the need for more rigorous research in this area. Therefore, further randomized controlled trials are necessary to better understand VR's impact on SCI patients' rehabilitation and to identify optimal training strategies and software.

Conclusions

This study conducted a quantitative analysis of the effects of VR intervention on the rehabilitation of SCI patients. The findings revealed that VR positively impacted the standing movement function and balance function. However, this study indicates that there was no significant improvement in lower limb motor function and activities of daily living in SCI patients before and after VR training. Given the limited literature on VR intervention for SCI patients and the absence of randomized controlled trials, future research demands large-scale, high-quality randomized controlled trials to delve deeper into the role of VR in SCI rehabilitation.

Abbreviations

SCI	Spinal cord injury
VR	Virtual reality
RCT	Randomized controlled trials
WISCI	The walking index for spinal cord injury
EMS	Extremity motor score
BBT	Box and block test
10WMT	10-meter walk test
BBS	Berg balance scale
LOS	Limits of stability testing
TUG	Timed up and go test
OR	Odds ratio
CI	Credible interval
MD	Mean difference
SMD	Standardized mean difference
CG	Comparison group
IG	Intervention group
ASIA	American spinal injury association impairment scale
OT	Occupational therapy
UEMS	Upper extremity motor score
LEMS	Lower extremity motor score
SCIM	Spinal cord independence measure

Supplementary Information

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Supplementary Material 1

Supplementary Material 2

Supplementary Material 3

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Not applicable.

Author contributions
WLk and LYX contributed to the study design, literature search, and data analysis. ZH conducted data extraction, and AHB provided critical feedback on data analysis. WLK drafted the manuscript, and LYX provided critical revisions to the manuscript for important intellectual content. LYX provided guidance on all aspects of the study. All authors have read and approved the final version of the manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
All authors have approved this manuscript for publication. This manuscript has not previously been published and is nor pending publication elsewhere.

Competing interests
The authors declare no competing interests.

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