REVIEW

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Virtual reality for limb motor function, balance, gait, cognition and daily function of stroke patients: A systematic review and meta-analysis

Bohan Zhang¹ | Dan Li² | Yue Liu¹ | Jiani Wang³ | Qian Xiao¹

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¹School of Nursing, Capital Medical University, Beijing, China

²School of Nursing, University of Pittsburgh, Pittsburgh, USA

³Fuwai Hospital, CAMS & PUMC, Beijing, China

Correspondence

Qian Xiao, School of Nursing, Capital Medical University, Beijing 100069, China. Email: julia.xiao@163.com

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Abstract

Aims: To explore the beneficial effects of virtual reality (VR) interventions on upperand lower-limb motor function, balance, gait, cognition and daily function outcomes in stroke patients.

Design: A systematic review and meta-analysis of randomized controlled trials.

Data Sources: English databases (PubMed, EMBASE, the Cochrane Library, CINAHL, Web of Science, Physiotherapy Evidence Database, ProQuest Dissertations and Theses) and Chinese databases (Chinese BioMedical Literature Service System, WANFANG, CNKI) and the Clinical Trial Registry Platform were systematically searched from inception until December 2019. Additionally, reference lists of the included studies were manually searched.

Review Methods: The methodological quality of studies was scored with the Cochrane 'risk-of-bias tool' and PEDro scale from the Physiotherapy Evidence Database by two independent evaluators.

Results: In total, 87 studies with 3540 participants were included. Stroke patients receiving VR interventions showed significant improvements in Fugl-Meyer assessment of Upper Extremity, Action Research Arm Test, Wolf Motor Function Test, Fugl-Meyer Assessment of Lower Extremity, Functional Ambulation Classification, Berg Balance Scale, Time Up and Go, Velocity, Cadence, Modified Barthel Index and Functional Independence Measure. However, differences between VR intervention and traditional rehabilitation groups were not significant for Box-Block Test, 10 m Walk Test, Auditory Continuous Performance Test, Mini-Mental State Examination and Visual Continuous Performance Test.

Conclusion: This review suggests that VR interventions effectively improve upperand lower-limb motor function, balance, gait and daily function of stroke patients, but have no benefits on cognition.

Impact: This review identified the positive effects of VR-assisted rehabilitation on upperand lower-limb motor function, balance, gait and daily function of stroke patients. And, we verified the duration of VR intervention affects some health benefits. The benefit of VR on cognitive function requires further investigation through large-scale multicentre RCTs.

KEYWORDS

balance, cognition, gait, limb motor function, meta-analysis, nursing, stroke, systematic review, virtual reality

1 | INTRODUCTION

Stroke is the most common neurological disease (Park et al., 2019) accounting for nearly a third of deaths worldwide (Wang et al., 2017). Up to 50% of stroke survivors are chronically disabled (Foley et al., 2012), leading to severe effects on daily activities and quality of life of patients. Cognitive and motor impairment and loss of balance and gait are the main factors affecting independent function and activity participation of stroke patients. Due to the complexity of stroke, nurses not only need to meet the role of therapeutic nursing, but also need to work with multidisciplinary teams to promote patients' rehabilitation (Aadal et al., 2013), such as supporting and respecting different rehabilitation needs in their interaction with patients (Kvigne et al., 2005), encourage stroke patients to do rehabilitation, help rehabilitation therapist adjust the rehabilitation plan, and then assist patients to re-enter social life more quickly (Dreyer et al., 2016).

Traditional rehabilitation programs usually face limitations in that training quantity and intensity are less rigorous than guidance (Foley et al., 2012) and enthusiasm for participation is low (Kaur et al., 2012). Virtual reality (VR) is a technology with interactive simulation creating a near-reality environment for users (Rose et al., 2018). VR technology is effectively used not only in diagnosis and teaching but also rehabilitation training (Huang et al., 2018; Ögün et al., 2019), and has been increasingly applied for stroke rehabilitation, intervention activities that need repetition, and specific tasks to improve limb function recovery after stroke (Park et al., 2019). Nurses can use VR equipment to change the clinical environment (Edwards, 2006), create a safer training environment to provide better rehabilitation support and bedside care (Kirkevold, 2010), and enhance the enthusiasm of patients to actively participate in rehabilitation (White et al., 2013). Moreover, VR can provide a richer experience for participants, making the rehabilitation process entertaining and engaging (Laver et al., 2012).

Due to the diversity of VR intervention results, meta-analysis of the evidence is needed to reveal the effects of VR rehabilitation on upper- and lower-limb, balance, gait, cognition and daily function of stroke patients, to explore the effects of different duration of VR intervention on health benefits, and then to provide theoretical basis for follow-up VR rehabilitation.

1.1 | Background

Stroke is the second most common fatal disease in the world (Chen et al., 2018). With the increase of the older population, the incidence of the disease is increasing year by year. Almost 17 million new strokes are reported worldwide each year (Virani et al., 2020). The prevalence rate of stroke in the United States is about 2.5% (Virani et al., 2020). According to stroke screening data, the standardized incidence of the first stroke in Chinese people aged 40–70 increased from 198/100,000 in 2002 to 379/100,000 in 2013, with an average annual growth rate of 8.3% (Institute for Health Metrics & Evaluation, 2017). The recurrence rate one year after the first stroke was as high as 17.1% (Guan

et al., 2017). Stroke is caused by poor cerebral blood flow, and there are two main types of stroke: haemorrhagic stroke and ischemic stroke (Jun-Long et al., 2018). Among them, ischemic stroke accounts for 80% of all strokes (Della-Morte et al., 2012).

The prognosis of stroke depends heavily on complications. Patients are often accompanied by complications such as chronic functional impairment and cognitive impairment. The fatality rate at 1 month and 5 years after stroke is about 15% and 50%, respectively (Hankey, 2017; Kernan et al., 2014). Stroke is the leading cause of long-term disability worldwide and dyskinesia is the most common damage after stroke, which exists in 85% of patients with acute stroke (Rathore et al., 2002). It is estimated that 55%-75% of post-stroke patients have functional limitations of the upper- and lower-limbs (Chen et al., 2019). 50%-60% of patients experience varying degrees of motor dysfunction after stroke (Hendricks et al., 2002). Among 2/3 of stroke patients have cognitive decline in different areas, including attention, memory, and executive function (Liu et al., 2017). Due to post-stroke patients have functional and cognitive impairment, functional tasks and daily activities are limited, which may lead to a decline in health-related guality of life (Hankey et al., 2002; Nichols-Larsen et al., 2005).

VR is an interactive computer-generated experience in a simulated environment, which mainly includes auditory and visual feedback (Liu et al., 2019). In recent years, VR technology has been mainly used in clinical rehabilitation (Kannan et al., 2019; Lee, 2019; Oh et al., 2019). VR can provide a more exciting and richer environment than traditional rehabilitation (Mirelman et al., 2013). Therefore, in theory, VR is a potentially beneficial intervention for rehabilitation training in stroke patients. In recent years, accumulating randomized controlled trials (RCTs) have been conducted to compare the effects of VR and traditional rehabilitation intervention programs in stroke patients. Virtual reality technology is reported to be more effective than traditional rehabilitation in improving the upper limb function and hand muscle injury of stroke patients (Choi et al., 2016; Oh et al., 2019). However, according to the reports of Hung et al. (2019) and Kim et al. (2018), both VR and traditional rehabilitation improved upper limb movement function of stroke patients, with no significant differences between the two intervention groups. Another study by Jiang and co-workers showed that VR could improve functional recovery of the upper limb, but had no significant positive effect on functional recovery of wrist and hand or upper limb movement in stroke patients (Jiang, 2017). Conflicting results on lower limb rehabilitation, balance, gait and cognition have been obtained from different studies (Aminov et al., 2018; Bergmann et al., 2018; Liao & Wang, 2014; Zhong et al., 2019). These discrepancies may be attributable to variations in the virtual reality technology and equipment used, the difficulty of VR games used, exercise duration and treatment methods.

Results from RCTs and meta-analyses in the literature are inconsistent. Aminov et al. (2018) reported a positive impact of VR on the upper limb of Fugl-Meyer motor function score (FMA-UE), Functional Independence Measure (FIM), Box-Block Test (BBT) and other parameters in stroke patients. In contrast, the meta-analysis of Zhong et al. (2019) confirmed a positive impact of VR on FMA-UE of stroke hemiplegic patients, but not BBT or FIM. In a systematic review by De Keersmaecker et al. (2019), VR improved the lower extremity balance ability of stroke patients, with significant differences in recorded Time Up and Go test (TUG) scores. In contrast, another systematic review by Perrochon et al. (2019) reported that VR had no major effect on the balance ability of stroke patients. Distinct results on gait and balance function were obtained by the research groups of Wang et al. (2019), Lee et al. (2019) and Casuso-Holgado et al. (2018). These inconsistent findings may be explained by differences in study design, post-stroke time and VR devices. Therefore, the actual benefits of VR as a measure of rehabilitation exercise in stroke patients remain to be established.

In addition, the effects of different duration of VR intervention on the functional recovery of patients are still unclear. According to the study of Han et al. (2017), when the duration of aerobic exercise is 8–12 weeks, it can better improve the cardiopulmonary fitness of patients. When the exercise time lasts for more than 4 weeks, it can be of the greatest benefit to the improvement of cognitive function, balance ability and endurance of stroke patients (Han et al., 2017). The same conclusion was reached in the study of Kim et al. (2019). However, Laver et al. (2017) found that there was no significant difference in the recovery of upper limb function in stroke patients with different treatment duration.

Therefore, this systematic review and meta-analysis was performed by comprehensive searching of English and Chinese electronic databases (from inception until 31 December 2019), strictly including RCT studies and assessing 16 outcome measures, to further evaluate the effectiveness of VR on upper- and lower-limb motor, balance, gait and cognition and explore the effects of different duration of VR intervention on functional recovery of stroke patients.

2 | METHODS

2.1 | Aims

The aim of this systematic review and meta-analysis was to evaluate the effects of VR on limb motor function, balance, gait, cognition and daily function of stroke patients, and to identify whether the duration of VR intervention affects health benefits.

2.2 | Design

This systematic review was registered at the website of International Prospective Register of Systematic Reviews and conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).

2.3 | Search methods

English and Chinese electronic databases were comprehensively searched from inception until 31 December 2019, including

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PubMed, EMBASE, the Cochrane Library, Physiotherapy Evidence Database (via the PEDro website), CINAHL, ProQuest, Web of Science, ProQuest Dissertations and Theses, Chinese BioMedical Literature Service System, WANFANG, CNKI, and Clinical Trial Register Platform. The search terms used were 'stroke', 'cerebrovascular disorders', 'virtual reality', 'user-computer interface' and their synonyms or translation in Chinese. The reference lists of included studies were additionally reviewed.

Studies were included with the following criteria: (1) population: stroke patients over 18 years of age, (2) design: RCT, (3) intervention: VR rehabilitation therapy, and (4) control: conventional rehabilitation or placebo therapy.

Studies were excluded based on the following criteria: (1) full text was unavailable, (2) incomplete information (unable to get the required data), (3) protocol, (4) duplicate records, (5) studies written in languages other than English or Chinese.

2.4 | Outcome measures

Sixteen outcomes were examined: (1) recovery of limb movement and function using Upper Extremity Fugl-Meyer assessment (FMA-UE), Action Research Arm Test (ARAT), Wolf Motor Function Test (WMFT), Box-Block Test (BBT), Lower Extremity Fugl-Meyer Assessment (FMA-LE), and Functional Ambulation Classification (FAC), (2) balance and gait using Berg Balance Scale (BBS), 10 m Walk Test (10MWT), Time Up and Go (TUG), and Velocity and Cadence scores, (3) cognition using Mini-Mental State Examination (MMSE), Auditory Continuous Performance Test (ACPT), Visual Continuous Performance Test (VCPT), (4) daily function using Functional Independence Measure (FIM) and Modified Barthel Index (MBI).

2.5 | Search outcome

Initially, a total of 9948 related studies were identified. Among these, 6499 duplicate records were removed, 3313 studies were excluded following screening of the title and abstract, 25 did not meet the inclusion criteria, and 24 were protocols or contained incomplete information. Finally, 87 RCTs (53 in English and 34 in Chinese) were included for meta-analysis. A flow diagram of the literature screening process is illustrated in Figure 1.

2.6 | Quality appraisal

The risk of bias of the included studies was assessed with the Cochrane 'risk-of-bias tool' (Jonathan, 2011) by the two researchers. The criteria included: (1) allocation concealment, (2) random sequence generation, (3) blinding of outcome assessment, (4) blinding of participants and personnel, (5) incomplete outcome data, (6) selective reporting, and (7) any other bias. Each study was classified as having 'low', 'high' or 'unclear' risk of bias.

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The quality of the included studies was also evaluated using the Physiotherapy Evidence Database (PEDro) Scale (Maher et al., 2003). The PEDro scale included 11 items, and its score depended on whether such items are met by the included studies. Each satisfied item (except the first one) contributes 1 point to the total score, which ranged from 0 to 10 points. The total score was divided into three level: (1) high quality (score 6–10), (2) fair quality (score 4–5) and (3) poor quality (score \leq 3).

2.7 | Study selection and data extraction

Two researchers independently selected studies using the specified inclusion and exclusion criteria. After screening the title and abstract, the full texts of the potentially eligible studies were further evaluated. We extracted the following data: title, published year, published journal, first author, sample size, research design, baseline characteristics of participants, intervention measures and outcomes. The third reviewer was involved in resolving the discrepancies between the two researchers.

2.8 | Data synthesis and analysis

Review Manager Software Revman (version 5.3) was applied for data processing and analysis. The l^2 test was used to analyse heterogeneity.

At p > .1 and $l^2 < 50\%$, the included studies were considered homogeneous and the fixed-effects model was used to analyse the pooled results. At $l^2 > 50\%$, the source of heterogeneity was assessed, focusing on the data extraction method, clinical intervention measures, research design, sensitivity, and other factors. The random-effects model was applied for further analysis. Subgroup analysis was conducted to explore the effects of different VR intervention duration (<4 weeks or ≥ 5 weeks) on health benefits. All outcomes were reported as mean difference (MD) and 95% confidence interval (CI). p values <.05 were statistically significant.

3 | RESULTS

3.1 | Study characteristics

In total, 87 studies including 3540 participants were reviewed (shown in Table 1). Among these studies, the average age of participants ranged from 46.3 to 72.8 years in the VR group and 47.5 to 76.4 years in the control group. The VR group contained 1029 males and 662 females, while the control group included 971 males and 687 females. Three studies had no information on gender. Overall, 852 and 812 cerebral infarction and 431 and 435 cerebral haemorrhage cases were identified in the VR and control groups, respectively. The mean time of onset to stroke ranged from 12.7 days to



FIGURE 1 Flow diagram of the literature screening process

18.4 years in the VR group and 13.2 days to 19.2 years in the control group.

3.2 | Risk of bias and quality

The risk of bias was presented in Figure S1. Overall, 32 studies did not report details of the random assignment method, while 24 studies used the allocation concealment process. Due to the limitations of experimental conditions, only three studies implemented blinding of participants. And blind method was implemented to outcome assessment in 33 studies. Furthermore, the risk of selective reporting and other bias was low.

The mean PEDro score assessing the methodological quality was 5.6 (SD 1.2), which ranged from 3 to 9 (Table 1). Among 87 studies, 32 studies (36.8%) were highlighted with high quality, and only one study was of low quality.

3.3 | Effectiveness of VR interventions

3.3.1 | Outcomes of upper limb movement and function

Thirty-eight studies (1773 participants) reported FMA-UE as an outcome. Moderate heterogeneity (p < .001, $I^2 = 67\%$) was observed among these studies. Results of meta-analysis using the random-effects model showed that the VR group had better FMA-UE scores than the control group (MD = 6.75, 95% CI = 5.58–7.93, p < .001; Figure 2a). Subgroup analyses disclosed significant differences in FMA-UE between the two groups regardless of whether the duration of the intervention period was ≤4 weeks or ≥5 weeks (Table 2).

Overall, 12 studies (541 participants) used BBT as an outcome measure. There was moderate heterogeneity among studies (p < .001, $l^2 = 70\%$) and the random-effects model was used for meta-analysis. No significant differences in BBT were observed between VR and control groups (MD = 1.73, 95% CI = -2.18-5.64, p = .13; Figure 2b). Subgroup analyses were further conducted to determine the effects of the duration of intervention on BBT. The two groups showed no significant differences in BBT irrespective of the length of the intervention period (≤ 4 or ≥ 5 weeks; Table 2).

Four studies (213 participants) focused on ARAT as an outcome. Meta-analysis with the fixed-effects model showed a greater improvement in ARAT in the VR intervention relative to the control group (MD = 7.18, 95% CI = 4.27–10.08, p < .001; Figure 2c). No significant homogeneity was observed among these studies (p = .18, $l^2 = 38\%$).

Six studies (317 participants) reported WMFT as an outcome. Pooled results obtained with the fixed-effects model showed that VR intervention exerted a greater effect on WMFT than traditional rehabilitation (MD = 4.43, 95% CI = 2.46-6.40, p < .001; Figure 2d). The included studies showed no heterogeneity (p = .13, $l^2 = 41\%$). 3.3.2 | Outcomes of lower limb movement and function

In total, 16 studies including 732 participants assessed FMA-LE. Significant heterogeneity among the studies was observed (p < .001, $l^2 = 77\%$) and the random-effects model used for analysis. The results showed a greater beneficial effect of VR rehabilitation on FMA-LE compared with traditional intervention (MD = 3.01, 95% CI = 1.91-4.11, p < .001; Figure 2e). Subgroup analyses further revealed that VR intervention over both ≤ 4 and ≥ 5 week periods had a significant positive effect on FMA-LE (Table 2).

Five studies (260 participants) reported FAC. High heterogeneity was observed across the remaining studies (p = .003, $I^2 = 75\%$). The random-effects model used for meta-analysis disclosed better FAC scores in the VR than control group (MD = 0.47, 95% CI = 0.14–0.79, p = .005; Figure 2f).

3.3.3 | Outcomes of balance and gait

In total, 21 studies (633 participants) evaluated BBS as an outcome measure. High heterogeneity was observed among the studies (p < .001, $l^2 = 80\%$). The pooled results obtained with the random-effects model revealed that VR influenced BBS to a greater extent than control intervention (MD = 3.51, 95% Cl = 2.10–4.92, p < .001; Figure 3a). Subgroup analyses showed that VR intervention delivered over both ≤ 4 and ≥ 5 weeks had significant positive effects on BBS (Table 2).

Seventeen studies (457 participants) used TUG as an outcome. VR had a greater effect in improving TUG (MD = -2.10, 95% CI = -3.52 to -0.73, p = .003; Figure 3b). We observed moderate heterogeneity among these studies (p < .001, $l^2 = 64\%$) and the random-effects model was used for meta-analysis. Interestingly, subgroup analyses showed a significant difference in TUG between the VR and control groups when the duration of intervention was ≤ 4 weeks, but no significant differences over ≥ 5 week periods (Table 2).

Four studies (138 participants) reported 10MWT. No significant differences between the VR and control groups were evident (MD = -1.45, 95% CI = -6.89-3.98, p = .60; Figure 3c) with the fixed-effects model. Heterogeneity was low (p = .29, $l^2 = 20\%$) among these studies.

Nine studies (310 participants) provided data on gait velocity. We observed no heterogeneity in these studies (p = .85, $l^2 = 0\%$) and the fixed-effects model was used for meta-analysis. The VR group was more improved than the control intervention group in terms of velocity (MD = 11.79, 95% Cl = 8.48–15.11, p < .001; Figure 3d). Subgroup analyses further showed that VR interventions (both ≤ 4 weeks and ≥ 5 weeks) exerted significant positive effects on gait velocity.

In total, nine studies (262 participants) evaluated gait cadence. Due to the low heterogeneity of the included studies (p = .12, $l^2 = 37\%$), pooled results were obtained with the fixed-effect model, which revealed that the VR group improved cadence to a better extent than the control group (MD = 8.35, 95% CI = 4.54–12.16,

			Participants					
Autho	r, Year	Country	Intervention/ Control (<i>n</i> / <i>n</i>)	Intervention	Control	Dosage	Outcomes included in this review	PEDro
1	Fei Huang (2019)	China	30/30	BioMaster VR interactive training	Conventional OT training	70–100min/d 5d/w,8w	FMA-UE	D.
7	Kuijie Fu (2019)	China	18/18	STB-110 VR training	Routine cognitive rehabilitation	30min/d 6d/w,4w	MMSE	5
т	Kyeongjin Lee, (2019)	Korea	21/21	Speed-interactive pedaling training with stationary bike by MOTOmed viva	Conventional therapy	40min/d 5d/w,6w	FMA-LE, Gait (Cadence)	6
4	Lakshmi Kannan (2019)	USA	13/12	Cognitive-motor exergame training by Wii Fit	Conventional balance training	ów, 20sessions	BBS, TUG	4
2	Lei Xu (2019)	China	30/30	VR-assisted training using GaitWatch	Regular rehabilitation training	20min/d 6d/w,6w	FMA-LE, FAC, Gait (Velocity, Cadence)	5
\$	Lu Fang (2019)	China	30/30	VR training using Xbox360	Conventional occupational therapy	15min/d 5-6d/w,12w	BBS	5
7	Mina Park (2019)	Korea	12/13	VR-based rehabilitation with Smart Board	Conventional rehabilitation	60min/d 5d/w,4w	MBI	7
8	Muhammed Nur ÖGÜN (2019)	Turkey	33/32	Upper extremity immersive VR rehabilitation program with Leap Motion	Conventional therapy	60min/d 3d/w,6w	FMA-UE, ARAT, FIM	6
6	Shuang Chen (2019)	China	20/20	VR rehabilitation therapy by Motekforce link	Traditional physical rehabilitation therapy	40min/d 5d/w,12w	FMA-LE, BBS Gait (Velocity, Cadence)	7
10	Xiang Xiao (2019)	China	16/19	VR training by Kinect somatosensory interaction	Conventional OT training	40min/d 5d/w,4w	FMA-UE, MBI	6
11	Yijin Zhao (2019)	China	35/35	VR training by BioMaster and Flextable	Conventional Occupational therapy training	50min、d 5d/w,4w	FMA-UE, MBI	6
12	Young-Bin Oh (2019)	Korea	17/14	Joystim for the VR combined with real instrument training	Standardized treatment program	30min/d 3d/w,6w	FMA-UE, BBT, MMSE	7
13	Zhibin Li (2019)	China	25/25	Upper limb intelligent feedback training system	Conventional OT training	45min/d 6d/w,4w	FMA-UE, WMFT, MBI	5
14	Ayça UTKAN KARASU (2018)	Turkey	12/11	Balance exercise with Wii Fit and Wii Balance Board	Conventional balance rehabilitation exercise	20min/d 5d/w,4w	BBS, TUG	7
15	Chunxia He (2018)	China	20/20	Upper limb intelligent feedback training system	Scapula motion control training	20 ~ 60min/d 5d/w	FMA-UE	5
16	Fang Lu (2018)	China	20/20	Lokomat training robot with VR	Conventional rehabilitation therapy	60min/d 5d/w,4w	FMA-LE, FAC	5
17	Huanxia Zhou (2018)	China	30/30	BioMaster virtual reality interactive training	Routine rehabilitation	30min/time 2time/d,6w	FMA-UE, MBI	5
18	Jaeho Park (2018)	Korea	12/16	Virtual reality robot-assisted gait training by Lokomat	Gait training using a treadmill	45min/d 3d/w,6w	FMA-LE, TUG, BBS, MBI	2

 TABLE 1
 Characteristics of the included studies

(Continues)

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	PEDro	ω	4	5	ω	9	6	Ø	5	4	5	6	6	5	2J	5	5	5	5	Continues)
	Outcomes included in this review	BBT	FMA-UE	FMA-UE, WMFT	FMA-UE, FIM	FMA-UE, BBT	FMA-LE, BBS, 10MWT, Gait (Velocity, Cadence)	FMA-UE, BBT, MBI	FMA-UE	FMA-LE	FMA-UE and FMA-LE, MMSE	FMA-LE, BBS, 10MWT	ARAT, BBT, FIM	MBI	FMA-UE and FMA-LE, BBS, MBI	FMA-UE, MMSE, MBI	FMA-UE, MBI	FMA-UE, MBI	MMSE	0)
	Dosage	60min/d 8-40sessions	40min/d 5d/w,12w	60min/d 6d/w,2w	2h/d 5d/w,4w	60min/d 5d/w,12w	30-40min/d 7d/w,4w	30min/d 5d/w,2w	30min/d 5d/w,2w	20min/d 5d/w,4w	50min/d 4-6d/w,4w	30min/d 7d/w,6w	60min/d 4 ~ 5d/w,4w	60min/d 5d/w,2w	30min/d 3d/w,12w	30min/d 5d/w,6w	60min/d 5d/w,8w	45min/d 5d/w,10w	20min/d 2-3d/w,12w	
	Control	Physical therapy	Traditional rehabilitation therapy	OT training	Conventional rehabilitation	Conventional therapy for upper extremity	Routine rehabilitation training	Conventional OT for upper limb recovery	Conventional PT	Routine rehabilitation training	Conventional intervention	Conventional PT	Conventional training	conventional rehabilitation training	Routine rehabilitation therapy	Routine cognitive tasks	Conventional therapy	Routine rehabilitation training	Conventional rehabilitation	
	Intervention	iMCR intervention individualized prescription of the repetitive exercises	VR training using virtual reality games by Wii	Kinect gaming and OT training	VR rehabilitation with a 3-dimensional motion tracking system	Xbox Kinect game system	Kinect-based VR rehabilitation training	Kinect-based VR for upper limb recovery	VR Wii game training	Four limbs combined with VR by Motek Medical	VR rehabilitation and cognitive intervention by Wii	Kinect-based VR training	VR training with the YouGrabber system	VR game training with Neuro-X	Virtual somatosensory exercise training by Wii	Cognitive training scenarios using Rehabilitation Gaming System set-up	Virtual kitchen rehabilitation training	BioMaster VR interactive training	Virtual simulation of a city-Reh@City	
Participants	Intervention/ Control (n/n)	35/38	12/12	21/22	68/68	19/16	20/20	11/8	18/18	15/15	33/33	10/10	57/55	25/25	48/48	6/5	67/67	20/20	6/6	
	Country	Australia	Korea	China	Italy	Turkey	China	Korea	China	China	China	Korea	Norway	Korea	China	Spain	China	China	Portugal	
	hor, Year	John Cannell (2018)	Ju-Hong Kim (2018)	Junzhi Zhu (2018)	Pawel Kiper (2018)	Sevgi Ikbali Afsar (2018)	Wenfeng Li (2018)	Won-Seok Kim (2018)	Xiaoxiao Han (2018)	Yana Li (2018)	Yanqun Hu (2018)	Dae-Sung Park (2017)	Iris Brunner (2017)	Kyeong Woo Lee (2017)	Liang Li (2017)	Martina Maier (2017)	Qian Zhu (2017)	Qing Liu (2017)	Ana Lúcia Faria (2016)	
	Aut	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	

TABLE 1 (Continued)

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	PEDro	7	7	5	Ŋ	5	Ŋ	2	5	6	4	ო	4	5	ω	5	7	5	2J	Continues)
	Outcomes included in this review	WMFT, BBT, FIM, MBI	FMA-UE	FMA-UE, FIM	FMA-UE, MBI	FMA-LE, BBS, TUG, FMA	BBS, TUG	FMA-UE, WMFT	FMA-LE, Gait (Velocity)	TUG, Gait (Velocity, Cadence)	BBS, TUG	TUG	BBS, TUG	BBS, FAC, TUG, MBI	BBS	FMA-LE, FAC, MBI	FIM	FMA-UE, MBI	FMA-UE)
	Dosage	60min/d 5d/w,2w	60min/d 7d/w,4w	60min/d 4d/w,3w	80min/d 6d/w,4w	30min/d 3d/w,4w	30min/d 5d/w,4w	40min/d 5d/w,4w	45min/d 5d/w,4w	30min/d 5d/w,6w	60min/d 3d/w,4w	30min/d 5d/w,8w	45min/d 3d/w,6w	30min/d 5d/w,2w	60min/d 5d/w,4w	30min/d 7d/w,4w	44–60min/d 3d/w,10w	45min/d 5d/w,6w	20 ~ 30min/d 6d/w,4w	
	Control	Recreational activity	Occupational therapy training	PT and OT	Routine rehabilitation therapy	Conventional rehabilitation program	Conventional rehabilitation program	Routine rehabilitation therapy	Routine rehabilitation training	Conventional PT	Conventional exercise training	Training using an ergometer bicycle	Proprioceptive neuromuscular facilitation	Conventional PT	Conventional therapy	Routine rehabilitation training	Routine therapy program	Routine therapy	Routine therapy	
	Intervention	VR using the Nintendo Wii gaming system	VR training by RAPAEL Smart Glove	Virtual game training by Wii Sports	VR training using the sling device	Canoe game-based virtual reality training program by Wii Sports Resort	Virtual reality reflection therapy	Virtual game training by Xbox Kinect	Virtual reality training by BioMaster	Virtual environment system ankle exercise by X-note	Wii Fit balance training	Performed training using the Xbox Kinect	VR exercise by BioRescue	VR training with BalPro	VR-based training	Virtual reality training by BioMaster	Virtual games training by Wii sports and Wii Fit packages	Virtual reality training by Bometric Ltd	BioMaster virtual reality interactive training	
Participants	Intervention/ Control (<i>n/n</i>)	71/70	24/22	33/35	30/30	5/5	13/12	20/20	40/40	10/10	15/15	20/20	10/10	23/17	10/10	40/40	20/22	17/17	28/28	
	Country	Canada	Korea	Singapore	China	Korea	Korea	China	China	Korea	Cyprus	Korea	Korea	Korea	Spain	China	Turkey	China	China	
	or, Year	Gustavo Saposnik (2016)	Joon-Ho Shin (2016)	Keng-He Kong (2016)	Lili Miao (2016)	Myung-Mo Lee (2016)	Taesung In (2016)	Wangxiang Mai (2016)	Yanwei Liu (2016)	Changho Yom (2015)	Gozde lyigun Yatar (2015)	Gui Bin SonG (2015)	In-Wook Lee (2015)	Jin Seok Huh (2015)	Llorens Rodríguez (2015)	Peishun Chen (2015)	Tülay Tarsuslu Simsek (2015)	Wenjun Pang (2015)	Xiaochuan Rong (2015)	
	Auth	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	

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	PEI	5	9	Ŋ	Ŋ	2	\sim	5	8	7	4	2	Ŋ	2	œ	9	, 2	5 (Conti
	Outcomes included in this review	FMA-UE	FMA-UE, ARAT	FMA-LE, 10MWT	BBT	FMA-UE, MBI	TUG	FMA-UE, MBI	FMA-UE, BBT, MMSE, ACPT, VCPT, MBI	BBS, TUG, Gait (Velocity, Cadence)	FMA-LE, TUG	FMA-UE, MBI	FMA-UE, FIM	FMA-UE, MBI	BBS	BBT	FMA-LE, Gait (Cadence), 10MWT	Gait (Velocity)
	Dosage	45min/time 2times/d 5d/w,8w	30min/d 3d/w,4w	20-30min/d 6d/w,4w	55min/d 5d/w,4w	30min/d 6d/w,8w	30mind 2d/w,12w	30min/d 5d/w,2w	30min/d 5d/w,4w	30min/d 3d/w,6w	30min/d 5d/w,8w	40min/d 5d/w,3w	60min/d 5d/w,4w	60min/d 5d/w,4w	45min/d 3d/w,8w	30min/d, 5d/w,6w	20–40min/d 5d/w,3w	30min/d 6d/w,2w
	Control	Routine therapy	Conventional reach exercises	Routine treatment	Conventional PT	Motor imagery therapy	Routine rehabilitation training	Occupational therapy	Conventional occupational therapy	Standard rehabilitation	Conventional robot training	Conventional occupational therapy	Traditional stroke rehabilitation	Routine rehabilitation	Conventional physical therapy	bilateral upper extremity training	Conventional physiotherapy	Conventional physiotherapy
	Intervention	Virtual reality training by Wii	Rehabilitation game by FurballHunt	VR training with BIOMaster	VR reflection equipment	Virtual reality training by BioMaster	Wii Fit VR training	VR by RehabMaster	Commercial gaming-based VR therapy using Wii	Treadmill walking training by JT-400 based real-world video recording	Virtual reality robot training system	Virtual kitchen training	VR Rehabilitation System by 3D motion- tracking system	Virtual reality technology training	VR training by Kinect	Bilateral upper extremity VR training	VR-enhanced body weight-supported training by Vicon Nexus	VR training
Participants	Intervention/ Control (n/n)	30/30	8/10	30/28	12/12	20/19	13/15	<i>2/9</i>	10/10	15/15	21/21	30/30	23/21	17/17	15/15	10/8	10/10	15/15
	Country	China	Netherlands	China	Korea	China	China	Korea	Korea	Korea	China	China	Italy	China	Spain	Korea	China	China
	or, Year	Yezhu Yang (2015)	Anke I. R. Kottink (2014)	Cuihua Liu (2014)	Dong Jin Lee (2014)	Hua Wu (2014)	Jen-Wen Hung (2014)	Joon-Ho Shin (2014)	Jun Hwan Choi (2014)	Ki Hun Cho (2014)	Linrong Liao (2014)	Ming Liang (2014)	Pawel Kiper (2014)	Qian Yu (2014)	Roberto Lloréns (2014)	Suhyun Lee (2014)	Xiang Xiao (2014)	Yijin Zhao (2014)
	Autho	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	20	71

TABLE 1 (Continued)

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		Outcomes included in this review	BBS	FIM	FMA-UE, BBT	BBS, TUG, Gait (Velocity, Cadence)	BBS, TUG	FMA-UE, MBI	Gait (Velocity, Cadence)	FMA-UE	ARAT	WMFT	BBS, TUG	FMA-UE, BBT, WMFT	FAC, TUG, BBS, MBI	FMA-UE, BBT	MMSE, MBI, ACPT, VCPT	MBI
		Dosage	25min/d 3d/w,3w	60min/d 3d/w,6w	30min/d 1d/w,6w	90min/d 5d/w,6w	60min/d 2d/w,5w	40min/d 5d/w,3w	60min/d 5d/w,4w	30min/d 5d/w,4w	30 ~ 45min/d 3d/w,3w	60min/d 5d/w,4w	90min/d 5d/w,6w	45min/d 3d/w,3w	20min/d 5d/w,4w	30min/d 5d/w,4w	30min/d 2d/w,4w	20min/d
		Control	Conventional balance training	Conventional OT	Conventional occupational therapy	PT and OT	Conventional PT	Traditional occupational therapy	Conventional PT	Conventional occupational therapy	Conventional arm therapy	Traditional therapy	Conventional PT and OT	Conventional therapy	Conventional PT	Conventional therapy	Computer-based cognitive rehabilitation	Occupational therapy
		Intervention	VR treatment by IREX	Training using video games played on the Xbox Kinect	Virtual reality training using Xbox-Kinect	Virtual walking training program with real- world video recording (VRRW)	Balance training with visual biofeedback using Wii Fit	Virtual kitchen upper extremities training	Virtual Reality-based postural control program	Virtual reality training by IREX VR system on upper extremity function	VR training	VR-based training by IREX	VR balance training by Wii	Goal-directed tasks via virtual games and virtual supermarket	VR training by Balance Control Trainer	Virtual Reality Reflection Therapy program	VR- and computer-based cognitive rehabilitation with IREX system	Rehabilitation Gaming system by Wii
	Participants	Intervention/ Control (n/n)	10/10	<i>T\T</i>	18/17	7 /7	10/10	16/17	8/8	13/13	6/6	15/14	11/11	8/6	20/20	11/8	15/13	8/8
		Country	Korea	Korea	Korea	Korea	Brazil	China	Korea	Korea	N	Koera	Korea	Canada	Korea	Korea	Korea	Spain
.E 1 (Continued)		or, Year	Yoon Bum Song (2014)	GyuChanG Lee (2013)	HyeonHui Sin (2013)	Ki Hun Cho (2013)	Luciana Barcala (2013)	Ming Liang (2013)	Yu-Hyung Park (2013)	Jae-Sung Kwon (2012)	JH Crosbie (2012)	Kihoon Jo (2012)	Ki Hun Cho (2012)	Mindy F. Levin (2012)	So Hyun Lee (2012)	Tae Sung In (2012)	Bo Ryun Kim (2011)	Mónica da Silva Cameirao
TABL		Auth	72	73	74	75	76	77	78	79	80	81	82	83	84	85	86	87

Functional Independence Measure; FMA, Fugl-Meyer assessment; FMA-LE, lower-extremity Fugl-Meyer Assessment; FMA-UE, upper extremity Fugl-Meyer assessment; MBI, Modified Barthel Index; MMSE, Mini-Mental State Examination; OT, occupational therapy; PT, physical therapy; TUG, Time UP and Go; VCPT, Visual continuous performance test; VR, virtual reality; WMFT, Wolf motor function test. Note

FIGURE 2 Forest plot showing limb movement and function

(a) Upper extremity Fugl-Meyer assessment (FMA-UE)

	VR rehabilitation		tion	Conventio	nal rehabili	tation		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Anke I.R. Kottink 2014	45	14	8	37	23	10	0.4%	8.00 [-9.24, 25.24]	
Chunxia He 2018	51.09	8.04	20	37.03	7.58	20	3.0%	14.06 [9.22, 18.90]	
Fei Huang 2019	46.2	7.15	30	36.24	7.39	30	3.8%	9.96 [6.28, 13.64]	
Hua Wu 2014	40.8	7.7	20	32.7	5.5	19	3.4%	8.10 [3.92, 12.28]	
Huanxia Zhou 2018	48.2	18.62	30	35.8	16.91	30	1.3%	12.40 [3.40, 21.40]	
HyeonHui Sin 2013	47.72	15.34	18	34.59	20.72	17	0.8%	13.13 [1.00, 25.26]	
Jae-Sung Kwon 2012	62.92	3.45	13	61.85	4.54	13	4.3%	1.07 [-2.03, 4.17]	
Joon-Ho Shin 2014	51.1	7.8	9	40.7	9.8	7	1.4%	10.40 [1.53, 19.27]	
Joon-Ho Shin 2016	58.3	1.7	24	49.6	2.7	22	5.6%	8.70 [7.38, 10.02]	+
Ju-Hong Kim 2018	55.42	11.61	12	49	10	12	1.4%	6.42 [-2.25, 15.09]	
Jun Hwan Choi 2014	40.3	18.4	10	47.2	10.5	10	0.7%	-6.90 [-20.03, 6.23]	
Junzhi Zhu 2018	49.86	4.62	21	47.09	5.08	22	4.4%	2.77 [-0.13, 5.67]	
Keng-He Kong 2016	32.8	18.2	33	30.3	17.8	35	1.4%	2.50 [-6.06, 11.06]	
Liang Li 2017	49.62	13.52	48	40.91	11.9	48	2.8%	8.71 [3.61, 13.81]	
lii Miao 2016	38.7	10.07	30	34.07	11.83	30	2.6%	4.63 [-0.93, 10.19]	
Martina Maier 2017	50.17	12.83	6	51.8	26.19	5	0.2%	-1.63 [-26.78, 23.52]	
Mindy F. Levin 2012	47.3	11.9	8	44.9	11.7	6	0.8%	2.40 [-10.08, 14.88]	
Ming Liang 2013	39.75	8.13	16	37.41	7.12	17	2.8%	2.34 [-2.89, 7.57]	
ding Liang 2014	45.97	6.3	30	40.33	8.23	30	3.8%	5.64 [1.93, 9.35]	
duhammed Nur ÖGÜN 2019	46.54	7.91	33	40.06	8.33	32	3.6%	6.48 [2.53, 10.43]	
Pawel Kiper 2014	49.8	12.5	23	49.5	16.2	21	1.4%	0.30 [-8.31, 8.91]	
Pawel Kiper 2018	47.71	15.74	68	46.29	17.25	68	2.6%	1.42 [-4.13, 6.97]	
Qian Yu 2014	45.93	20.58	17	35.26	14.49	17	0.8%	10.67 [-1.29, 22.63]	
Dian Zhu 2017	57.51	11.51	67	43.6	10.17	67	3.8%	13.91 [10.23, 17.59]	
Ding Liu 2017	58	5.71	20	47.85	4.07	20	4.3%	10.15 [7.08, 13.22]	
Sevgi Ikbali Afsar 2018	43.05	12.59	19	34.44	10.53	16	1.7%	8.61 [0.95, 16.27]	
Fae Sung In 2012	59.45	7.42	11	49.57	12.95	8	1.1%	9.88 [-0.11, 19.87]	
Nangxiang Mai 2016	46.85	5.16	20	41.95	5.95	20	4.0%	4.90 [1.45, 8.35]	
Venjun Pang 2015	56.88	4.53	17	50.76	3.4	17	4.6%	6.12 [3.43, 8.81]	
Non-Seok Kim 2018	50.1	14.3	11	45.5	17.3	8	0.6%	4.60 [-10.07, 19.27]	
Kiang Xiao 2019	32.98	11.24	16	30.23	10.13	19	1.9%	2.75 [-4.40, 9.90]	
Gaochuan Rong 2015	57.89	11.46	28	43.92	10.32	28	2.5%	13.97 [8.26, 19.68]	
Gaoxiao Han 2018	34.86	6.32	18	29.09	4.5	18	3.9%	5.77 [2.19, 9.35]	
rangun Hu 2018	43.3	5.2	33	36.6	6.2	33	4.5%	6.70 [3.94, 9.46]	
rezhu Yang 2015	37.01	2.34	30	28.51	12.52	30	3.2%	8.50 [3.94, 13.06]	
rijin Zhao 2019	48.37	1.38	35	43.43	1.07	35	6.0%	4.94 [4.36, 5.52]	-
roung-Bin Oh 2019	39.5	15.1	17	38.6	18.5	14	0.8%	0.90 [-11.16, 12.96]	
Zhibin Li 2019	42.44	6.8	25	35.88	6.29	25	3.8%	6.56 [2.93, 10.19]	
						070	100.00	0.7515 50.7.001	
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 Total (95% CI)
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 Heterogeneity: Tau² = 5.97; Chi² = 113.52, df = 37 (P < 0.00001); I² = 67%

 Test for overall effect: Z = 11.25 (P < 0.00001)</td>

-20 -10 0 10 20 Favours VR rehabilitation FavoursConventional rehabilitation

(b) Box-Block Test (BBT)

	VRre	habiitat	tion	Convention	nal rehabilit	ation		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl
DongJin Lee 2013	24	13.99	12	15.42	12.75	12	7.3%	8.58 [-2.13, 19.29]	
Gustavo Saposnik 2016	27.2	15.5	71	30.9	13.2	70	12.9%	-3.70 [-8.45, 1.05]	
HyeonHui Sin 2013	20.67	14.38	18	16.29	11.7	17	8.9%	4.38 [-4.28, 13.04]	
Iris Brunner 2017	26	18.7	57	25	19.1	55	10.5%	1.00 [-6.00, 8.00]	
John Cannell 2018	23.5	2.7	35	27.8	1.7	38	15.8%	-4.30 [-5.35, -3.25]	•
Jun Hwan Choi 2014	26.6	17.5	10	29.6	11	10	5.9%	-3.00 [-15.81, 9.81]	
Mindy F. Levin 2012	30.3	27.7	8	23.9	21.2	6	2.0%	6.40 [-19.22, 32.02]	
Sevgi Ikbali Afsar 2018	28.53	11.15	19	20.81	10.01	16	10.5%	7.72 [0.71, 14.73]	
Suhyun Lee 2014	35.79	14.51	10	15.63	13.19	8	5.9%	20.16 [7.34, 32.98]	
Tae Sung In 2012	16.91	9.76	11	16.29	10.55	8	8.4%	0.62 [-8.69, 9.93]	
Won-Seok Kim 2018	13.3	13.1	11	13	13.4	8	6.3%	0.30 [-11.79, 12.39]	
Young-Bin Oh 2019	25.1	15.4	17	29.7	21.2	14	5.6%	-4.60 [-17.90, 8.70]	
Total (95% CI)			279			262	100.0%	1.73 [-2.18, 5.64]	+
Heterogeneity: Tau ² = 24.9	34: Chi ² :	36.55.	df = 11	(P = 0.0001)	P = 70%				
Test for overall effect: Z = I	0.87 (P =	0.39)							-50 -25 0 25 50
									Favours [VR renabilitati] Favours [Conventional rehabilitation]

(C) Action Research Arm Test (ARAT)

	VRrel	abiitat	ion	Conventio	onal rehabili	tation		Mean Difference	Mean D	ifference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixe	d, 95% Cl		
Anke I.R. Kottink 2014	45	14	8	41	18	10	3.9%	4.00 [-10.78, 18.78]	-	•		
Iris Brunner 2017	37.7	19.5	57	36.8	18.8	55	16.8%	0.90 [-6.19, 7.99]		+		
JH Crosbie 2012	52.8	6.9	9	50.2	18.9	9	4.9%	2.60 [-10.54, 15.74]	-	-		
Muhammed Nur ÖGÜN 2019	41.15	7.82	33	32.09	5.94	32	74.4%	9.06 [5.69, 12.43]				
Total (95% CI)			107			106	100.0%	7.18 [4.27, 10.08]		•		
Heterogeneity: Chi ² = 4.85, df =	3 (P = 0.1	18); I ² =	38%						-100 -50	0	50	100
Test for overall effect: Z = 4.84 (i	P < 0.000	JO1)							Favours (experimental	Favours (o	control]	

(d) Wolf motor function test (WMFT)

	VRrel	abiitat	tion	Convention	nal rehabili	tation		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Gustavo Saposnik 2016	45.5	26	71	50.6	22.8	70	5.9%	-5.10 [-13.17, 2.97]	
Junzhi Zhu 2018	49.52	6.19	21	46.45	5.3	22	32.4%	3.07 [-0.38, 6.52]	
Kihoon Jo 2012	35.3	11.9	15	28	5.3	14	8.8%	7.30 [0.67, 13.93]	
Mindy F. Levin 2012	54.3	16.1	8	53.2	20	6	1.0%	1.10 [-18.41, 20.61]	
Wangxiang Mai 2016	44.55	6.32	20	39.5	5.56	20	28.4%	5.05 [1.36, 8.74]	
Zhibin Li 2019	48.36	7.49	25	41.32	7.15	25	23.4%	7.04 [2.98, 11.10]	
Total (95% CI)			160			157	100.0%	4.43 [2.46, 6.40]	•
Heterogeneity: Chi ² = 8.48	, df = 5 (F	= 0.13	3); I ² = 4	1%					20 10 0 10 20
Test for overall effect: Z = -	4.42 (P <	0.0000	1)						Favours (experimental) Favours (control)

(e) Lower-extremity Fugl-Meyer Assessment (FMA-LE)

	VR rel	habiitat	ion	Convention	al rehabilitat	ion		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% CI
Cuihua Liu 2014	31.52	1.85	30	29.46	3.41	28	8.1%	2.06 [0.63, 3.49]	
Dae-Sung Park 2017	26.1	7.31	10	27.5	5.19	10	2.8%	-1.40 [-6.96, 4.16]	
Fang Lu 2018	22.45	3.33	20	17.65	3.31	20	7.1%	4.80 [2.74, 6.86]	
Jaeho Park 2018	30.16	1.57	12	26.25	2.29	16	8.1%	3.91 [2.48, 5.34]	
Kyeongjin Lee 2019	19.49	3.56	21	18.59	2.72	21	7.3%	0.90 [-1.02, 2.82]	
Lei Xu 2019	19.03	4.32	30	15.51	4.88	30	6.6%	3.52 [1.19, 5.85]	
Liang Li 2017	28.33	7.15	48	23.62	5.96	48	6.1%	4.71 [2.08, 7.34]	
Linrong Liao 2014	29.24	2.01	21	26.24	2.86	21	8.0%	3.00 [1.50, 4.50]	
Myung-Mo Lee 2016	39.8	3.1	5	31.2	9.1	5	1.4%	8.60 [0.17, 17.03]	
Peishun Chen 2015	29.23	4.37	40	19.48	6.36	40	6.5%	9.75 [7.36, 12.14]	
Shuang Chen 2019	28.8	1.66	10	25.2	1.48	10	8.2%	3.60 [2.22, 4.98]	
Wenfeng Li 2018	28.02	9.76	20	29.45	6.32	20	3.1%	-1.43 [-6.53, 3.67]	
Xiang Xiao 2014	24.4	4.67	10	26.57	5.88	10	3.5%	-2.17 [-6.82, 2.48]	
Yana Li 2018	22.18	1.83	15	21.57	3.13	15	7.5%	0.61 [-1.22, 2.44]	
Yangun Hu 2018	29.9	2.3	33	27.8	3.1	33	8.3%	2.10 [0.78, 3.42]	
Yanwei Liu 2016	25.17	4.05	40	21.85	5.21	40	7.1%	3.32 [1.27, 5.37]	
Total (95% CI)			365			367	100.0%	3.01 [1.91, 4.11]	•
Heterogeneity: Tau ² = 3	3.35; Chi ²	= 64.0	7, df = 1	5 (P < 0.000)	01); I ² = 77%				
Test for overall effect: Z	= 5.35 (F	< 0.00	001)						-20 -10 0 10 20

(f) Functional Ambulation Classification (FAC)

	VR rel	abiitat	ion	Convention	al rehabilit	ation		Mean Difference	Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl	
Fang Lu 2018	2.65	0.88	20	1.45	1	20	14.8%	1.20 [0.62, 1.78]		
Jin Seok Huh 2015	3.2	0.7	23	3.31	0.48	17	21.0%	-0.11 [-0.48, 0.26]	+	
Lei Xu 2019	2.67	0.76	30	2.27	0.52	30	22.1%	0.40 [0.07, 0.73]	+	
Peishun Chen 2015	3.28	0.52	40	2.79	0.34	40	26.0%	0.49 [0.30, 0.68]	•	
So Hyun Lee 2012	4	0.7	20	3.4	1	20	16.1%	0.60 [0.07, 1.13]	-	
Total (95% CI)			133			127	100.0%	0.47 [0.14, 0.79]	◆	

The terrogeneity: Tau² = 0.10; Chi² = 15.84, df = 4 (P = 0.003); P = 75% Test for overall effect: Z = 2.83 (P = 0.005)

-4 -2 0 2 4 Favours [VR rehabilitation] Favours [Conventional rehabilitation]

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TABLE 2 Meta-Analysis of the effects of virtual reality on stroke patients

							Subgroup ana	lysis	
Outcomes	Number of studies	Number of participants	Heterogeneity	MD	95%CI	р	Intervention duration	MD (95%CI)	р
FMA-UE	38	1773	$I^2 = 67\%, p < .001$	6.75	5.58 to 7.93	<.001	≤4 weeks	5.30 (4.01 to 6.59)	<.001
							≥5 weeks	9.12 (7.48 to 10.75)	<.001
BBT	12	541	$I^2 = 70\%, p < .001$	1.73	-2.18 to 5.64	.13	≤4 weeks	-0.69 (-3.86 to 2.49)	.67
							≥ 5 weeks	6.83 (-0.88 to 14.54)	.08
ARAT	4	213	$I^2 = 38\%, p = .18$	7.18	4.27 to 10.08	<.001	≤4 weeks	1.69 (-4.06 to 7.45)	.56
							≥5 weeks	-	_
WMFT	6	317	$I^2 = 41\%, p = .13$	4.43	2.46 to 6.40	<.001	-	-	-
FMA-LE	16	732	$I^2=77\%, p<.001$	3.01	1.91 to 4.11	<.001	≤4 weeks	2.72 (0.52 to 4.93)	.02
							≥ 5 weeks	3.30 (2.35 to 4.25)	<.001
FAC	5	260	$I^2 = 75\%, p = .003$	0.47	0.14 to 0.79	.005	≤4 weeks	0.50 (0.06 to 0.94)	.03
							≥5 weeks	-	_
BBS	21	633	$I^2 = 80\%, p < .001$	3.51	2.10 to 4.92	<.001	≤4 weeks	4.40 (1.58 to 7.22)	.002
							≥5 weeks	2.81 (1.23 to 4.40)	<.001
TUG	17	457	$I^2 = 64\%, p < .001$	-2.10	-3.52 to -0.73	.003	≤4 weeks	-2.48 (-4.03 to -0.92)	.002
							≥ 5 weeks	-1.81 (-3.78 to 0.17)	.07
10MWT	4	138	$I^2 = 20\%, p = .29$	-1.45	-6.89 to 3.98	.60	≤4 weeks	-1.32 (-6.98 to 4.35)	.65
							≥5 weeks	_	_
Gait	9	310	$I^2 = 0\%, p = .85$	11.79	8.48 to 15.11	<.001	≤4 weeks	10.16(6.40 to 13.92)	<.001
velocity							≥ 5 weeks	17.48(10.45 to 24.51)	<.001
Gait	9	262	$I^2 = 37\%, p = .12$	8.35	4.54 to 12.16	<.001	≤4 weeks	2.46 (-3.41 to 8.33)	.41
cadence							≥ 5 weeks	12.64 (7.63 to 17.64)	<.001
MMSE	7	210	$I^2 = 66\%, p = .007$	0.81	-0.41 to 2.03	.19	≤4 weeks	1.02 (0.21 to 1.83)	.01
							≥ 5 weeks	0.52 (-2.40 to 3.44)	.73
ACPT	2	48	$I^2 = 87\%, p = .006$	0.03	-0.12 to 0.17	.74	-	-	_
VCPT	2	48	$I^2 = 40\%, p = .20$	-0.03	-0.09 to 0.02	.20	-	-	-
MBI	27	1315	$I^2=72\%, p<.001$	7.02	4.96 to 9.08	<.001	≤4 weeks	6.71 (4.16 to 9.25)	<.001
							≥5 weeks	8.03 (3.77 to 12.29)	<.001
FIM	8	622	$I^2 = 18\%, p = .29$	2.52	0.32 to 4.72	.02	≤4 weeks	0.62 (-2.35 to 3.58)	.68
							≥5 weeks	4.93 (1.65 to 8.22)	.003

p <.001; Figure 3e). Subgroup analyses showed no marked differences in cadence between the two groups for intervention periods ≤ 4 weeks, while differences were significant at ≥ 5 weeks (Table 2).

3.3.4 | Outcomes of cognition

Seven studies (210 participants) evaluated MMSE as an outcome and showed no significant differences between VR and control groups (MD = 0.81, 95% CI = -0.41-2.03, p = .19; Figure 4a). Heterogeneity was moderate (p = .007, $l^2 = 66\%$) and the random-effects model used for meta-analysis. Subgroup analyses showed significant differences in MMSE scores between the two groups for intervention periods ≤ 4 weeks but not ≥ 5 weeks (Table 2).

ACPT was reported in two studies (48 participants). No significant differences were observed between VR and control groups (MD = 0.03, 95% CI = -0.12-0.17, p = .74; Figure 4b) with the random-effects model. Heterogeneity was high (p = .006, I^2 = 87%).

VCPT was evaluated in two studies (48 participants) with low heterogeneity (p = .20, $l^2 = 40\%$). No significant differences in were observed between VR and control groups (MD = -0.03, 95% CI = -0.09-0.02, p = .20; Figure 4c) with the fixed-effects model.

3.3.5 | Outcomes of daily function

Twenty-seven studies (1315 participants) described the effects of VR relative to control interventions on MBI. Differences in

	VRre	ehabiitat	tion	Convention	nal rehabilr	tation		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl
Ayça UTKAN KARASU 2018	48.9	6.4	12	42.2	6.4	11	3.5%	6.70 [1.46, 11.94]	
Dae-Sung Park 2017	50	6.27	10	44.7	7.47	10	3.0%	5.30 [-0.74, 11.34]	
Gozde lylGun yatar 2015	50.33	4.09	15	44.8	7.48	15	4.2%	5.53 [1.22, 9.84]	
In-Wook Lee 2015	46.2	2.3	10	41.5	3.7	10	5.5%	4.70 [2.00, 7.40]	
Jaeho Park 2018	50.16	1.72	12	45.75	1.91	16	6.4%	4.41 [3.06, 5.76]	-
Jin Seok Huh 2015	44.3	6.63	23	42.38	4.86	17	4.8%	1.92 [-1.64, 5.48]	
Ki Hun Cho 2014	42.6	3.06	15	41.06	5.29	15	5.2%	1.54 [-1.55, 4.63]	
Ki Hun Cho 2012	43.09	4.8	11	43.9	4.06	11	4.6%	-0.81 [-4.53, 2.91]	
Ki Hun Cho 2013	40.85	1.67	7	37	3.21	7	5.5%	3.85 [1.17, 6.53]	
Lakshmi Kannan 2019	49.31	2.65	13	49.45	4.655	12	5.2%	-0.14 [-3.14, 2.86]	
Liang Li 2017	47.63	13.31	48	43.56	13.18	48	3.5%	4.07 [-1.23, 9.37]	
Llorens Rodríguez 2015	51	4.6	10	46.2	5.7	10	4.0%	4.80 [0.26, 9.34]	
Lu Fang 2019	47.1	9.7	30	43.1	10.7	30	3.6%	4.00 [-1.17, 9.17]	
Luciana BarcaLa 2013	41.9	6.91	10	42.2	4.8	10	3.5%	-0.30 [-5.51, 4.91]	
Myung-Mo Lee 2016	46.2	4.3	5	41.2	2.9	5	4.0%	5.00 [0.45, 9.55]	
Roberto Lloréns 2014	51.2	2.11	15	51.07	5.09	15	5.4%	0.13 [-2.66, 2.92]	
Shuang Chen 2019	46.3	1.89	10	39.9	2.02	10	6.2%	6.40 [4.69, 8.11]	
So Hyun Lee 2012	45.7	7.8	20	41.7	6.9	20	4.0%	4.00 [-0.56, 8.56]	
Taesung In 2016	49.08	2.72	13	46.08	2.97	12	5.8%	3.00 [0.76, 5.24]	
Wenfeng Li 2018	48.32	1.76	20	39.45	2.32	20	6.5%	8.87 [7.59, 10.15]	+
Yoon Burn Song 2014	48.3	3.5	10	47.9	2.3	10	5.6%	0.40 [-2.20, 3.00]	+
Total (95% CI)			319			314	100.0%	3.51 [2.10, 4.92]	◆
Heterogeneity: Tau ² = 7.55; C	hi ² = 97 l	60 df=	20 (P <	0.00001): P	= 80%				
Test for overall effect: 7 = 4 8	B (P < 0.0	00001)	(-20 -10 0 10 20
		/							Favours IVR rehabilitation] Favours [Conventional rehabilitation]

(b) UP and Go (TUG)

ean Difference
Random, 95% Cl
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+
+
+
+
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-+
•
entall Eavours (control)

Favours [experimental] Favours [control]

(c) 10m Walk Test (10MWT)

	VRre	habiitat	tion	Convention	nal rehabili	tation		Mean Difference	Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI	_
Cuihua Liu 2014	57.58	24.31	30	50.36	23.59	28	19.4%	7.22 [-5.11, 19.55]	-+ -	
Dae-Sung Park 2017	44.73	20.7	10	47.77	22.98	10	8.0%	-3.04 [-22.21, 16.13]		
Wenfeng Li 2018	45.67	9.51	20	50.82	12.47	20	62.5%	-5.15 [-12.02, 1.72]		
Xiang Xiao 2014	56	19	10	50	20	10	10.1%	6.00 [-11.10, 23.10]		
Total (95% CI)			70			68	100.0%	-1.45 [-6.89, 3.98]		
Heterogeneity: Chi ² = 3. Test for overall effect: 7	.77, df = = 0.52 (3 (P = 0 P = 0.60	l.29); I*÷ N	= 20%					-100 -50 0 50 100	
reetter ereran eneou. 2	. 0.00	·/						Favours (experimental) Favours (control)		

(d) Velocity

	VRI	ehabiitati	ion	Conventional rehabilitation				Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% Cl
Changho Yom 2015	65.65	22.57	10	48.87	18.36	10	3.4%	16.78 [-1.25, 34.81]	
Ki Hun Cho 2014	74.16	19.73	15	58.33	20.53	15	5.3%	15.83 [1.42, 30.24]	
Ki Hun Cho 2013	79.67	13.91	7	61.8	20.64	7	3.2%	17.87 [-0.57, 36.31]	
Lei Xu 2019	63.47	24.63	30	42.97	26.84	30	6.5%	20.50 [7.46, 33.54]	
Shuang Chen 2019	67	16	10	52	22	10	3.9%	15.00 [-1.86, 31.86]	
Wenfeng Li 2018	66	7	20	55	10	20	38.4%	11.00 [5.65, 16.35]	+
Yanwei Liu 2016	68	12	40	57	23	40	17.0%	11.00 [2.96, 19.04]	
Yijin Zhao 2014	59.67	12.402	15	51.67	7.198	15	20.9%	8.00 [0.74, 15.26]	
Yu-Hyung Park 2013	59.94	21.33	8	50.59	33.84	8	1.4%	9.35 [-18.37, 37.07]	
Total (95% CI)			155			155	100.0%	11.79 [8.48, 15.11]	*
Heterogeneity: Chi ² = 4.07, df = 8 (P = 0.85); I ² = 0%									-100 -50 0 50 100
Test for overall effect: Z = 6.97 (P < 0.00001)								Favours I/R rehabilitation] Favours (Conventional rehabilitation)	

Favours [VR rehabilitation] Favours [Conventional rehabilitation]

(e) Cadence

	VR rel	abiitati	on	Convention	nal rehabilit	ation		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	CI IV, Fixed, 95% CI
Changho Yom 2015	103.46	12.45	10	83.6	22.92	10	5.6%	19.86 [3.69, 36.03]	3]
Ki Hun Cho 2014	99.64	14.55	15	84.76	19.26	15	9.7%	14.88 [2.66, 27.10]	0]
Ki Hun Cho 2013	104.04	10.01	7	89.82	17.32	7	6.6%	14.22 [-0.60, 29.04]	4] *
Kyeongjin Lee 2019	83.34	16.11	21	75.4	18.05	21	13.6%	7.94 [-2.41, 18.29]	9]
Lei Xu 2019	94.6	17.47	30	78.23	20.43	30	15.7%	16.37 [6.75, 25.99]	9]
Shuang Chen 2019	89.05	15.22	10	86.41	18.15	10	6.7%	2.64 [-12.04, 17.32]	2]
Wenfeng Li 2018	78.86	9.51	20	74.67	12.38	20	31.0%	4.19 [-2.65, 11.03]	3]
Xiang Xiao 2014	70.01	12.51	10	76.95	19.78	10	6.9%	-6.94 [-21.45, 7.57]	7]
Yu-Hyung Park 2013	80.39	15.95	8	75.29	21.31	8	4.3%	5.10 [-13.35, 23.55]	5)
Total (95% CI)			131			131	100.0%	8.35 [4.54, 12.16]	6]
Heterogeneity: Chi ² = 1	2.71, df =	8 (P = 1	0.12); l²	= 37%					-100 -50 0 50 100
Test for overall effect: 2	Z = 4.30 (F	< 0.00	01)						Favours [VR rehabilitation] Favours [Conventional rehabilitation]

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(a) Mini-Mental State Examination (MMSE)

	VR rel	habiitat	ion	Convention	al rehabili	tation		Mean Difference	Mean Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl		
Ana Lúcia Faria 2016	28	1.62	9	24.88	1.43	9	18.4%	3.12 [1.71, 4.53]			
Bo Ryun Kim 2011	21	4.6	15	22.1	5.4	13	7.4%	-1.10 [-4.85, 2.65]			
Jun Hwan Choi 2014	23.7	3.7	10	21.6	5.9	10	6.0%	2.10 [-2.22, 6.42]			
Kuijie Fu 2019	27	2	18	25.44	2.23	18	18.6%	1.56 [0.18, 2.94]			
Martina Maier 2017	27	1.1	6	27.8	2.39	5	13.2%	-0.80 [-3.07, 1.47]			
Yangun Hu 2018	26.8	1.9	33	26	2.5	33	20.6%	0.80 [-0.27, 1.87]			
Young-Bin Oh 2019	27.9	3.2	14	28.9	1.6	17	15.7%	-1.00 [-2.84, 0.84]			
Total (95% Cl)			105			105	100.0%	0.81 [-0.41, 2.03]	•		
Heterogeneity: Tau² = 1	.58; Chi²	= 17.79	9, df = 6		-10 -5 0 5 10						
Test for overall effect: Z	= 1.31 (F	P = 0.19)					Favours (experimental) Favours (control)			

(b)Auditory continuous performance test (ACPT)

	VR rel	habiitat	ion	Convention	al rehabilit	ation		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl
Bo Ryun Kim 2011	0.6	0.1	15	0.5	0.1	13	50.1%	0.10 [0.03, 0.17]	a
Jun Hwan Choi 2014	0.68	0.07	10	0.73	0.1	10	49.9%	-0.05 [-0.13, 0.03]	•
Total (95% CI)			25	-		23	100.0 %	0.03 [-0.12, 0.17]	· · · · ·
Heterogeneity: Tau* = 0 Test for overall effect: Z	1.01; Chi* = 0.34 (F	P = 0.74	,df=1 (l)	(P = 0.006); I*	= 87%				-2 -1 0 1 2 Favours [experimental] Favours [control]

(C) Visual continuous performance test (VCPT)

	VR rehabilitation Conventional rehabilitation							Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Bo Ryun Kim 2011	0.5	0.1	15	0.5	0.1	13	50.9%	0.00 [-0.07, 0.07]	
Jun Hwan Choi 2014	0.49	0.07	10	0.56	0.1	10	49.1%	-0.07 [-0.15, 0.01]	
Total (95% CI)			25			23	100.0%	-0.03 [-0.09, 0.02]	•
Heterogeneity: Chi ² = 1. Test for overall effect: Z	67, df = 1 = 1.27 (F	1 (P = 0 P = 0.20	1.20); l²:))	= 40%			-0.5 -0.25 0 0.25 0.5 Favours (experimental) Favours (control)		

(d) Modified Barthel Index (MBI)

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	VRre	habiitat	tion	Conventional rehabilitation				Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Bo Ryun Kim 2011	69.7	20.2	15	50.9	25.5	13	1.2%	18.80 [1.58, 36.02]	
Gustavo Saposnik 2016	83.4	18	71	80.3	21.7	70	4.0%	3.10 [-3.49, 9.69]	
Hua Wu 2014	69.1	11.2	20	59.6	10.1	19	3.9%	9.50 [2.81, 16.19]	
Huanxia Zhou 2018	58.4	13.71	30	43.57	11.91	30	4.0%	14.83 [8.33, 21.33]	
Jaeho Park 2018	67.33	6.69	12	62.5	4.22	16	5.2%	4.83 [0.52, 9.14]	
Jin Seok Huh 2015	79.35	10.4	23	80.38	7.88	17	4.4%	-1.03 [-6.70, 4.64]	
Joon-Ho Shin 2014	71.2	15.4	9	51	8.8	7	2.0%	20.20 [8.21, 32.19]	_
Jun Hwan Choi 2014	85	11.6	10	86.9	10.5	10	2.7%	-1.90 [-11.60, 7.80]	
Kyeong Woo Lee 2017	52.64	6.97	25	51.28	15.14	25	4.0%	1.36 [-5.17, 7.89]	
Liang Li 2017	68.55	15.72	48	65.96	14.06	48	4.3%	2.59 [-3.38, 8.56]	
Lili Miao 2016	70.17	10.07	30	65.67	11.72	30	4.5%	4.50 [-1.03, 10.03]	
Martina Maier 2017	88.33	10.8	6	95	11.18	5	1.8%	-6.67 [-19.74, 6.40]	
Mina Park 2019	74.9	16.8	12	76.5	15.5	13	1.9%	-1.60 [-14.30, 11.10]	
Ming Liang 2013	67.75	12.18	16	67.65	11.88	17	3.2%	0.10 [-8.12, 8.32]	
Ming Liang 2014	70.03	10.62	30	61.87	10.85	30	4.6%	8.16 [2.73, 13.59]	
Mónica da Silva Cameirao 2011	94.9	8.9	8	88	17.8	8	1.7%	6.90 [-6.89, 20.69]	
Peishun Chen 2015	60.12	14.68	40	40.25	14.75	40	4.0%	19.87 [13.42, 26.32]	
Qian Yu 2014	58.45	13.79	17	48.96	12.98	17	2.9%	9.49 [0.49, 18.49]	
Qian Zhu 2017	79.21	12.87	67	65.29	11.07	67	5.3%	13.92 [9.86, 17.98]	
Qing Liu 2017	61	7.68	20	49.25	5.8	20	5.2%	11.75 [7.53, 15.97]	
So Hyun Lee 2012	70.4	18	20	68.1	12.6	20	2.7%	2.30 [-7.33, 11.93]	
Wenjun Pang 2015	86.18	9.22	17	85.88	9.23	17	4.2%	0.30 [-5.90, 6.50]	
Won-Seok Kim 2018	83.2	10.2	11	67.5	1.3	8	4.2%	15.70 [9.61, 21.79]	
Xiang Xiao 2019	80.43	16.45	16	76.32	17.44	19	2.2%	4.11 [-7.14, 15.36]	
Xiaochuan Rong 2015	76.54	12.19	28	65.21	11.67	28	4.1%	11.33 [5.08, 17.58]	
Yijin Zhao 2019	79.57	1.78	35	74	1.43	35	6.6%	5.57 [4.81, 6.33]	+
Zhibin Li 2019	70.32	8.61	25	63.6	8.44	25	4.9%	6.72 [1.99, 11.45]	
Total (95% CI)			661			654	100.0%	7.02 [4.96, 9.08]	◆
Heterogeneity: Tau ² = 16.54; Chi ² :	= 93.94,	df = 26	(P < 0.0	0001); I ² = 7	2%				
Test for overall effect: Z = 6.68 (P <	0.0000	1)							-20 -10 0 10 20 Eavoure I/R rebabilitatil Eavoure (Conventional rebabilitation)

Favours [VR rehabilitati] Favours [Conventional rehabilitation]

(e) Functional Independence Measure (FIM)

	VRre	habiitat	tion	Conventional rehabilitation				Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Gustavo Saposnik 2016	108.8	16.2	71	106.1	17.6	70	15.5%	2.70 [-2.89, 8.29]	
GyuChanG Lee 2013	71.42	15	7	61.24	11.93	7	2.4%	10.18 [-4.02, 24.38]	
Iris Brunner 2017	107.7	14.6	57	108.7	14.3	55	16.9%	-1.00 [-6.35, 4.35]	
Keng-He Kong 2016	87.6	18.5	33	93.5	17.7	35	6.5%	-5.90 [-14.52, 2.72]	
Muhammed Nur ÖGÜN 2019	89.6	8.2	33	84.96	6.42	32	37.8%	4.64 [1.07, 8.21]	
Pawel Kiper 2014	103.3	22.9	23	104.6	18.2	21	3.3%	-1.30 [-13.47, 10.87]	
Pawel Kiper 2018	104.4	18.5	68	100.66	17.53	68	13.2%	3.74 [-2.32, 9.80]	
Tülay Tarsuslu Simsek 2015	111.7	15.06	20	107.09	19.24	22	4.5%	4.61 [-5.79, 15.01]	
Total (95% CI)	7/8=0	201-18-	312			310	100.0%	2.52 [0.32, 4.72]	◆
Test for overall effect: Z = 2.25 (P = 0.02	29),1"=	1070						-20 -10 0 10 20 Favours (VR rehabilitati) Favours (Conventional rehabilitation)

FIGURE 4 Forest plot showing cognition and daily function

MBI scores were significant between the groups (MD = 7.02, 95% CI = 4.96–9.08, p < .001; Figure 4d). Due to the moderate heterogeneity among studies (p < .001, $l^2 = 72\%$), the random-effects model was used. Subgroup analyses showed that VR intervention periods of both \leq 4 and \geq 5 weeks had significant positive effects on MBI.

FIM was reported in eight studies (622 participants) with low heterogeneity (p = .29, $l^2 = 18\%$). We observed significant differences in FIM between the VR and control groups (MD = 2.52, 95% CI = 0.32-4.72, p = .002; Figure 4e) with the fixed-effects model. Differences in FIM between the two subgroups were not significant for intervention periods <4 weeks but significant for interventions \geq 5 weeks (Table 2).

3.4 | Sensitivity analysis

Sensitivity analysis was conducted by omitting each study in turn and recalculating the pooled relative risks. No single study significantly influenced the overall results of FMA-UE, WMFT, BBT, FMA-LE, FAC, BBS, TUG, 10MWT, gait velocity and cadence, MMSE and MBI. However, the pooled data on ARAT and FIM were influenced by the study of Ögün et al. (2019), which showed that no significant differences in these outcome measures were evident between VR and control groups after removal of this study from the meta-analysis.

4 | DISCUSSION

To our knowledge, the current meta-analysis is the most comprehensive investigation examining the efficacy of VR in stroke rehabilitation to date, including 87 RCTs (3540 participants) with the assessment of 16 outcome indicators and subgroup analyses based on the duration of intervention. Our findings indicate that VR improves limb function, walking ability, balance, gait velocity, cadence, and daily life activities to a greater extent than conventional rehabilitation. However, VR had a similar effect on improvement of cognition as conventional rehabilitation therapy.

Virtual reality technology has '31' characteristics, specifically, immersion, interactivity and imagination (Subramanian & Prasanna, 2018). VR games have distinct clinical advantages compared with traditional therapies as they offer a challenging and interesting environment. The VR devices used in this study included Wii, BioMaster, Xbox Kinect, and Rapael Smart Board[™]. Our results suggest that VR intervention in a game form has beneficial effects on recovery of limb movement and function, consistent with the findings of Lee and Chun (2014) and Gibbons et al. (2016) In subgroup analysis of the effects of VR on limb function, FMA-UE and FMA-LE scores were improved regardless of the intervention duration. Moreover, longer periods of VR delivery were associated with greater improvement. VR is reported to improve fine motor activities and sensory feedback (Kim et al., 2018) but the finger function is not suitable for short-term rehabilitation and the shortest intervention duration that can exert therapeutic effects remains to be established.

The positive results of VR training in this study are consistent with data from previous meta-analyses on the effect of VR on the balance of stroke patients (Aminov et al., 2018). However, opposite findings were obtained in a systematic review by Casuso-Holgado et al. (2018), which only included 11 studies. BBS was the most frequent outcome evaluating the static and dynamic balance, which covered the key point of balance more fully than TUG. Some reviews have reported the positive findings in favour of VR as rehabilitation therapy (Mohammadi et al., 2019; Lee et al., 2019. Miyamoto and co-workers showed a strong correlation between BBS and TUG (Miyamoto et al., 2009). We additionally obtained compelling evidence on the effectiveness of VR in improving gait velocity and cadence in post-stroke patients. The gait characteristics of most stroke patients include shortening of the single leg support phase, hyperextension of the knee joint in the support phase, reduction of hip joint flexion in the affected side, foot drooping, and slowing down of gait speed (Zhao et al., 2014). Therefore, the main goals of gait training for stroke patients are to improve walking speed and posture. During gait training, the effectiveness of VR in improving gait function may be affected by the degree of immersion (i.e. non-, semi- or fully immersive). Recent studies have shown that more immersive VR systems are more beneficial for training, compared with less immersive systems (Menin et al., 2018; Tieri et al., 2018). However, the issue of whether the level of immersion is correlated with improvement in gait function remains to be established. In addition, our collective data suggest that a VR intervention period of least five weeks is required to obtain improve gait cadence to a greater extent than traditional rehabilitation.

The MBI and FIM were found to be better in VR group than that in the conventional rehabilitation group. This result suggested that VR induces a marked improvement in daily life function and self-care of patients, which may be attributed to the improvement of muscle strength through VR training (Lee, 2013). With the improvement of daily function, stroke patients' subjective well-being would also be gradually improved (Allen et al., 2002). From a long-term point of view, the improvement of daily function could not only reduce the rate of rehospitalization, but also an important predictor of hospital stays and mortality (Nunes & Queirós, 2017). Our results differ from those reported by Subramanian and Prasanna (2018) which only included two studies published in 2014 (Lee & Chun, 2014) and 2015(Zheng et al., 2015). In this article, research intervention design involved not only VR intervention alone but also VR in combination with non-invasive brain stimulation (Subramanian & Prasanna, 2018). Furthermore, compared with traditional rehabilitation, the advantages of VR on FIM were not evident until a period of >5 weeks. FIM is an 18-item measurement tool exploring physical, psychological and social functions that reflects the daily function of patients.

Cognitive impairment in stroke patients is common. However, the overall effects of VR on MMSE, ACPT and VCPT were not

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encouraging. The limited number of studies included for analysis may affect data on the advantages of VR rehabilitation. Our results showed no significant benefits of VR rehabilitation on cognition, compared with conventional rehabilitation therapy, consistent with the findings of Aminov et al. (2018). These findings may be attributed to the fact that cognitive function training is not the main purpose of current VR interventions. The lack of VR programs tailored for cognitive function training is the main reason for insufficient evidence to date. In addition, the result that VR had no significant effect on cognition may be have something to do with the assessment tools. Mini-Mental State Examination (MMSE), Auditory Continuous Performance Test (ACPT) and Visual Continuous Performance Test (VCPT) were used to evaluate the cognitive function of stroke patients. Although the American Academy of Neurology recommended MMSE as an important tool for detecting early cognitive impairment in its guidance (Petersen et al., 2001), many researchers doubt the accuracy of this scale (Ciesielska et al., 2016; Espino et al., 2001: Mitchell, 2009: Van et al., 2017). ACPT and VCPT were originally designed to detect persistent attention deficit in patients, they usually were used to assess patients' alertness and cognitive performance (Arble et al., 2014). Therefore, these two tools were more widely used in the assessment of attention deficit hyperactivity disorder in children, but rarely in the cognitive assessment of stroke patients. So, better assessment tools are needed to study the effect of VR on cognitive function in stroke patients in the future. Furthermore, impairment of cognitive function among stroke patients can lead to anxiety, fidgeting behaviours, and impairment of social functioning (Kim et al., 2019). Using different VR systems, patients can be trained in a comfortable, safe, and immersive environment, which may benefit cognitive ability (Sánchez et al., 2013). Further studies are required to ascertain the potential benefits of VR on cognition in stroke patients.

4.1 Study strengths and limitations

The main strength of this systematic review is that we analysed the effects of VR on upper- and lower-limb motor function, balance, gait, cognition and daily function of stroke patients, including 87 randomized controlled trials from 15 countries and regions, which was the most comprehensive systematic review to date. Second, we conducted a more rigorous quality assessment of included studies, using Cochrane 'risk-of-bias tool' and PEDro scale, respectively, both of which have their own focus and advantages. Third, we further identified whether the duration of VR intervention affects health benefits. Additionally, this systematic review was conducted in strict accordance with the guideline of PRISMA.

Our study has several limitations that may affect the interpretation of the results. First, the type of VR program used may influence rehabilitation progress. Subgroup analysis was difficult in this review due to the range of VR programs used in different studies. Further studies are needed to compare the effects of different VR intervention types. Second, differences in baseline

characteristics, form, dosage, and frequency of VR interventions resulted in increased heterogeneity among the included studies. According to the results of sensitivity analyses, no single study significantly influenced the overall results of most outcomes in this review. However, pooled data on ARAT and FIM were influenced by one study and the effects of VR on these parameters should be further examined via large-scale RCTs. In addition, this review failed to demonstrate the superiority of VR intervention over traditional training in terms of improvement in cognition, which may be attributed to the limited reports available that have focused on cognition as an outcome. Most VR projects to date have been focused on the rehabilitation of physical function, and effects on cognition thus require further evaluation.

5 CONCLUSIONS

Data from this review indicate that VR is more effective in improving limb function, walking ability, balance, gait velocity, cadence and daily function than conventional rehabilitation. The issue of whether VR has advantages over traditional interventions in terms of improving cognitive function requires further investigation through largescale multicentre RCTs.

AUTHOR CONTRIBUTIONS

Made substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data (BHZ, DL, YL, JNW, QX); Involved in drafting the manuscript or revising it critically for important intellectual content (BHZ, DL, YL, JNW, QX); Given final approval of the version to be published. Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content (BHZ, DL, YL, JNW, QX); Agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved (BHZ, DL, YL, JNW, QX).

CONFLICT OF INTEREST

No conflict of interest has been declared by the authors.

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PEER REVIEW

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DATA AVAILABILITY STATEMENT

The data that supports the findings of this study are available in the supplementary material of this article.

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ORCID

Qian Xiao 🕩 https://orcid.org/0000-0002-5657-2863

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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