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Virtual rehabilitation of upper extremity function and independence for stoke: a meta-analysis

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We aimed to conduct a systematic literature review with a meta-analysis to investigate whether virtual reality (VR) approaches have beneficial effects on the upper extremity function and independent activities of stroke survivors. Experimental studies published between 2007 and 2017 were searched from two databases (EBSCOhost and PubMed). This study reviewed abstracts and assessed full articles to obtain evidence on qualitative studies. For the meta-analysis, the studies that estimated the standardized mean between the two groups analyzed the statistical values necessary for calculating the effect size. The present study also evaluated the statistical heterogeneity. In total, 34 studies with 1,604 participants were included, and the number of participants in each study ranged from 10 to 376. Nine studies were assessed to evaluate the quantitative statistical analysis for 698 patients with hemiparetic stroke. The results of the meta-analysis were as follows: The overall effect size was moderate (0.41, $P<0.001$). The 95% confidence interval ranged from 0.25 to 0.57. However, no significant heterogeneity and publication bias were observed. The results of this study showed that VR approaches are effective in improving upper extremity function and independent activities in stroke survivors.

Keywords: Independence, Meta-analysis, Stroke, Upper extremity, Virtual reality

INTRODUCTION

Stroke has varying severity and subsequent functional impact, which depends on the recovery process of an individual and the extent of neurological damage (Chollet et al., 1991). Several stroke survivors experience physical, cognitive, perceptual, and mental impairments that require a period of intensive rehabilitation and may develop permanent disabilities (Teasell et al., 2005). Some stroke survivors can undergo a short period of inpatient rehabilitation program for recovery of function, and others continue to recover for a long period or throughout their lifetimes (Cramer, 2011). Therefore, in the intensive rehabilitation of individuals with neurological diseases, extremely important considerations must be made because of the reintegration of family and social roles and recreational activities (French et al., 2016; West and Bernhardt, 2012).

In rehabilitation settings, functional and task-specific trainings are the key elements of therapy and designed to assist stroke survivors in restoring their motor control to attain more-normal functional movement patterns (Teasell et al., 2005). Stroke survivors must have significant changes in the motor control and strength of the trunk and limbs, with an emphasis on the more-affected side and bilateral symmetric movement; these may be achieved using specific reeducation strategies (Veerbeek et al., 2014; West and Bernhardt, 2012). In terms of stroke rehabilitation settings, most previous studies were performed in laboratory or clinical settings that are less complex than the outdoor environment (Cho and Lee, 2013). Laboratory and clinical settings are not appropriate for establishing some complex personal space and community surroundings to meet the demands of multiple tasks for stroke survivors (Demain et al., 2013; Fung et al., 2012).

Virtual reality (VR) is a computer-generated environment that simulates a realistic experience for practicing functional tasks at intensities higher than those in traditional rehabilitation programs for stroke survivors (Chen et al., 2016). VR may help engage

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stroke survivors in a repetitive, intensive, and goal-oriented therapy to improve their functional disabilities, activity limitations, and participation restrictions, without considering the cost and burden associated with increasing the number of therapeutic sessions (Merians et al., 2002). Furthermore, VR provides real-time visual feedback for movements, thereby increasing engagement in enjoyable rehabilitation tasks. VR provides rehabilitative clinicians with new and effective therapeutic tools that can help treat various disabilities and enables remote therapy. VR-based interventions lead to clinical improvement and cortical reorganization through repetitive, adaptive, task-oriented, meaningful, and challenging exercises for stroke survivors (Laver et al., 2012).

As mentioned earlier, several virtual realities in rehabilitation interventions have been applied in the stroke population. However, the efficacy of VR rehabilitation interventions remains to be fully elucidated. In particular, studies on the qualitative and quantitative beneficial effects of VR on upper extremity function and independence in performing activities of daily living among patients with stroke are limited. The objectives of the present study were as follows: (a) to investigate the effectiveness of VR-based interventions in rehabilitation programs for restoring the upper extremity function of stroke survivors through a systematic review and (b) to examine the efficacy of VR-based interventions as part of a therapeutic rehabilitation program to improve upper limb function and independence in performing activities of daily living in stroke survivors by conducting a meta-analysis. Then, the VR-based interventions that are effective for improving upper limb function and independence in performing activities of daily living in stroke survivors were identified.

MATERIALS AND METHODS

Data sources and searches

A literature search of studies conducted between January 1, 2007, and August 31, 2017, was conducted using PubMed and EBSCOhost. The following key words were used: "hemiplegia" AND "virtual reality," "hemiplegic" AND "virtual reality," and "stroke" AND "virtual reality." These terms were used as key words in the title and abstract of the studies in all databases. All the articles were cautiously screened by two reviewers, who selected relevant articles to be included in the present study.

Study selection

Studies that (a) were published in the English language; (b) involved adult patients with stroke; (c) included adult patients with hemiparesis after stroke during the acute, subacute, and chronic phases; (d) used randomized controlled trials; (e) investigated any form of immersive or nonimmersive VR-based interventions; and (f) used specific outcome measures to assess upper extremity function were included in the study. For the meta-analysis in this study, the inclusion criteria were as follows: First, the study aimed to improve upper extremity function after stroke using VR-based interventions. Second, the outcome measure was independence in performing activities of daily living. Third, the study must use validated and standardized evaluation tools with objective measurement units to determine the degree of independence in performing activities of daily living.

Two authors independently assessed the studies for eligibility. Any disagreement in the study selection was resolved during consensus meetings. By using this method, 726 articles were identified. Studies that were in accordance with the inclusion criteria or those that could not be included on the basis of the content of the abstract were selected for a full-text review. The abstracts of the remaining publications were evaluated for eligibility by two independent assessors. The systematic review method identified 726 studies, of which 692 had insufficient data required for the analysis. Thus, 34 articles were included in the systematic review by both assessors (Fig. 1).

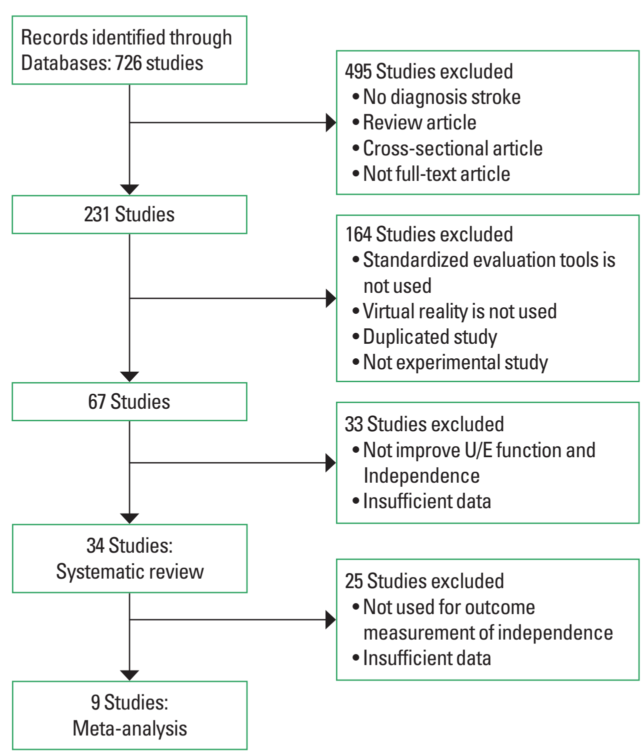

Fig. 1. Flow diagram of the search strategy. U/E, upper extremity.

Data extraction and quality assessments

The following data were extracted from the selected studies: diagnosis of the participants, age, study design, assessment, interventions, and operational definition. Finally, 34 studies were included. Nine studies were included in the meta-analysis. The following identifiable data were obtained from the studies: means and standard deviations, *t*-test results, and *P*-values (Table 1).

For the meta-analysis, the methodological quality of each study

Table 1. Characteristic of included studies for meta-analysis (n=9)

Study	Jadadscore	Participants	Intervention		Outcome measure	Outcome
			Intervention/groups	Session/time		
Piron et al., 2010	4	n=47 (experimental n=27/control n=20)	• Motor learning. based approach in a VR • Conventional upper ex tremity therapy	• 4 weeks, 5 days per week, with 1-hr treatment sessions daily	• FMA • FIM • Kinematic outcomes	Both rehabilitation therapies improved arm motor performance and functional activity.
da Silva Cameirão et al., 2011	3	n=16 (experimental n=8/control n=8)	• RGS • Control	• 3 weekly sessions of 20 min	• BI • Motricity Index • Muscle strength • FMA • CAHAI	Rehabilitation with the RGS facilitates the functional recovery of the upper extremities.
Turolla et al., 2013	1	n=376 (experimental n=113/control n=263)	• Combined VR and upper limb conventional therapy • Upper limb conventional therapy alone.	• 2 hr of daily therapy, 5 days per week, for 4 weeks.	• FMA • FIM	VR rehabilitation in post-stroke patients seems more effective than conventional interventions in restoring upper limb motor impairments.
Choi et al., 2014	4	n=20 (experimental n=10/control n=10)	• Commercial gaming-based VR therapy • Conventional OT	• 30 min a day for 4 weeks	• FMA • MFT • BBT • MBI • MMSE • Continuous performance test	The gaming-based VR therapy was as effective as conventional OT on the recovery of upper extremity motor and daily living function.
Kiper et al., 2014	3	n=44 (experimental n=23/control n=21)	• RFVE • Traditional rehabilitation	• 5 days weekly for 4 weeks	• FMA • FIM • Kinematics • Parameter	Some poststroke patients may benefit from RFVE program for the recovery of upper limb motor function.
Shin et al., 2014	4	n=16 (RehabMaster, OT n=8/OT only n=8)	• RehabMaster intervention plus conventional occupational therapy • Conventional occupational therapy only	• 30 min of RehabMaster per day for 2 weeks • 20 min of conventional occupational therapy plus RehabMaster	• FMA • MBI	The RehabMaster is a feasible and safe VR system for enhancing upper extremity function in patients with stroke.
Yin et al., 2014	1	n=23 (experimental n=11/control n=12)	• Upper extremity VR therapy in standing • Conventional therapy	• 30 min for 5 week days in 2 weeks	• FMA • ARAT • MAL • FIM	Although additional VR training was not superior to conventional therapy alone.
Zheng et al., 2015	3	n=112 (experimental n=58/control n=54)	Low-frequency rTMS and VR training, Sham rTMS and VR training	• 6 days per week for 4 weeks	• FMA • WMFT • MBI • SF-36	The combined use of LF rTMS with VR training could effectively improve the upper limb function, the living activity, and the quality of life.
Ballester et al., 2016	4	n=40 (experimental n=20/control n=20)	• Goal-oriented movement amplification in VR • Same training protocol without movement amplification.	• 30 min of daily for 6 weeks	• FMA • CAHAI • BI	This improvement was accompanied by a significant increase in arm-use during training in the experimental group.

ARAT, action research arm test; BI, Barthel index; CAHAI, Chedoke arm and hand activity inventory; FIM, functional independence measure; FMA, Fugl-Meyer assessment; MAL, motor activity log; MBI, modified Barthel index; MMSE, Mini-Mental State Examination; MMT, manual muscle testing; RGS, Rehabilitation Gaming System; RFVE, reinforced feedback in virtual environment; rTMS, repetitive transcranial magnetic stimulation; SF-36, 36-item short form health survey; VR, virtual reality; WMFT, Wolf motor function test.

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was assessed by two independent reviewers using the Jadad scale. The Jadad scale score was required for validating the quality of clinical trials, and blind raters assessed the quality to limit the risk of introducing bias into the meta-analyses and peer-review process. In addition, the nine articles were classified according to outcome measurements and the analysis of outcome measurements (Table 1).

Data synthesis and analysis

For the systematic review, the PICOS method was used to delineate the following five components of our literature review (Liberati et al., 2009): P (patient), adults who were diagnosed as having stroke; I (intervention), all types of VR-based interventions; C (comparison), rehabilitation intervention for a control group; and O (outcome), outcome measures for assessing upper extremity function and independence.

For the meta-analysis, Comprehensive Meta-Analysis version 2.0 (Biostat, Englewood, NJ, USA) was used to analyze the effect size, statistical heterogeneity, and publication bias in the selected studies. Effect size was calculated by dividing the ratio of the mean difference between the experimental and control groups by the standard deviation of the control group. The effect size for upper extremity function after stroke using VR-based interventions was determined using a standardized mean difference and 95% confidence intervals (CIs) in the fixed-effects model, which indicates the mean improvement in the standard scores of the experimental group relative to the control group.

Statistical heterogeneity refers to the degree of variation or inconsistency in the results of individual studies. Integrating research with different characteristics can lead to statistical heterogeneity and hence bias results; the heterogeneity of the studies was assessed using the Cochran *Q* test. Publication bias was assessed. A funnel plot and Egger regression interceptors were used. The funnel plot allows researchers to visually assess standard errors by reflecting the effect size on the horizontal axis.

RESULTS

Systematic review of studies

The study analyzed previous studies that evaluated the effects of VR-based interventions on upper extremity function after stroke. The 34 studies for systematic review included randomized controlled trials. A total of 1,507 patients with hemiplegic stroke were included. The mean number of participants was 678 in the VR-based intervention group and 829 in the control group. The experimental group consisted of a minimum of 5 participants and a maximum of 117 participants, whereas the control group had a minimum of 5 participants and a maximum of 268 participants.

Table 2. Frequency of outcome measurement

Outcome measurement	Frequency (%)
Upper limb function	
FMA	23 (54.8)
WMFT	5 (11.9)
MAL	5 (11.9)
Independence	
BI (MBI)	5 (11.9)
FIM	4 (9.5)
Total	42 (100)

FMA, Fugl-Meyer assessment; WMFT, Wolf motor function test; MAL, motor activity log; BI, Barthel index; MBI, modified Barthel index; FIM, functional independence measure.

The assessment tools used for the upper extremity functions were functional mobility assessment (FMA), Wolf motor function test (WMFT), and motor activity log (MAL). FMA was used in 23 studies; MAL, in 5 studies; and WMFT, in 5 studies. Meanwhile, the assessment tools used for assessing independence in performing activities of daily living were the Barthel index (BI) and functional independence measure (FIM). BI was used in 5 studies, and FIM was used in 4 studies (Table 2).

This study analyzed the types of VR interventions in 34 articles. The results are shown in Table 3. In terms of the VR-based interventions, VR systems that use computers, video games, and video capture and those with bilateral, goal-oriented, hand/arm, and reinforced feedback trainings were used in 20 studies. Six studies used games and Wii and Xbox, and two studies used robots. Furthermore, some studies used smart glove and smartphone programs, transcranial magnetic stimulation, RehabMaster, and the YouGrabber virtual system. On the basis of the results of this study, most VR-based interventions were related to upper extremity function and independence in performing activities of daily living in stroke patients.

Meta-analysis of the studies

The BI and FIM were used in the studies for meta-analysis, including 698 patients with hemiplegic stroke. The number of participants in each study ranged from 16 to 376. The methodological quality of the primary data was assessed using the Jadad scale score (Table 1). Three studies scored 1–4 of the maximum score of 4 points. The random assignments of the assessors were handled appropriately only in one study (Piron et al., 2010). Blinding of

Table 3. Characteristic of studies for systematic review except studies using a meta-analysis (n=25)

No.	Study	Patients (n)	Intervention		Outcome measure (primary)	Outcome
			Intervention/groups	Session/time		
1	Adie et al., 2017	n=235 (experimental group 117/control group 118)	• Wii • Arm exercises at home	• 45 min daily for 6 weeks	• ARAT • COPM • Stroke impact scale • Modified Rankin scale • EQ-5D 3L	The trial showed that the WiiTM was not superior to arm exercises in home-based rehabilitation for stroke survivors with arm weakness.
2	Broeren et al., 2008	n=22 (experimental group 11/control group 11)	• Received extra rehabilitation by training on a computer • Continued their previous rehabilitation without computer	• Computer 3 times a week during a 4-week period	• Semi-Structured Interview • BBT • ABILHAND • Trail making test	The usefulness of computer games in training motor performance.
3	Choi et al., 2014	n=24 (intervention group 12/control group 12)	• Mobile upper extremity rehabilitation program using a smartphone	• 60 min per day, 5 days per week, for 2 weeks	• FMA • Brunnstrom stage • MMT • MBI • EQ-5D • Beck Depression Inventory	
4	Crosbie et al., 2012	n=18 (experimental group 9/control group 9)	• VR group • Conventional arm therapy	• Nine sessions over 3 weeks	• Motoricity index • ARAT	VR-mediated therapy would be feasible, with some suggested improvements in recruitment and outcome measures.
5	Housman et al., 2009	n=28 (T-WREX group 14/control group 14)	• Therapy Wilmington Robotic Exoskeleton • Control (tabletop exercise)	• Twenty-four 1-hr treatment sessions and at 6-month follow-up	• FMA • ROM • MAL	Conventional and T-WREX treatment can lead to modest gains in patients with moderate to severe weakness with less than 4 min of direct therapist contact per hour of therapy.
6	Fluet et al., 2014	n=40 (experimental group 20/control group 20)	• Hand and arm separate training • Hand and arm together training	• Two hr of training on day 1, and progressed to 3 hr by day 4, which continued to day 8	• WMFT • Jebsen hand function test	Short term changes in upper extremity motor function were comparable when training the upper extremity with integrated activities or a balanced program of isolated activities.
7	Lee et al., 2014	n=18 (experimental group 10/control group 8)	• VR-based bilateral upper extremity training • Bilateral upper limb training	• 30 min day, 3 days a week, for a period of 6 weeks	• Jebsen hand function test • Grooved pegboard test • Hand strength test	VR-based training is a feasible and beneficial means of improving upper extremity function and muscle strength in individuals following stroke.
8	Lee et al., 2014	n=24 (experimental group 12/control group 12)	• Symmetric training program • Asymmetric training programs virtual reality reflection equipment	• 30 min/day, 5 day/wk, for 4 weeks	• FMA • BBT • ROM • Grip strength	The asymmetric training program using virtual reality reflection equipment is an effective intervention method for improving upper limb function in stroke patients.
9	Lee et al., 2016a	n=10 (experimental group 5/control group 5)	• Canoe game-based virtual reality training program • Conventional rehabilitation program	• 30 min, 3 days a week for 4 weeks	• FMA • TUG • BBS • System usability scale questionnaire • FRT • Trunk impairment scale	Canoe game-based virtual reality training is an acceptable and effective intervention for improving trunk postural stability, balance, and upper limb motor function in stroke patients.

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Table 3. Continued

No.	Study	Patients (n)	Intervention		Outcome measure (primary)	Outcome
			Intervention/groups	Session/time		
10	Levin et al., 2012	n=12 (experimental group 6/control group 6)	• 2D video-capture VR training • Conventional therapy	• 45-min intervention sessions over a 3-week period.	• FMA • Composite spasticity index • Reaching performance scale for stroke • BBT • WMFT • MAL	The modest advantage of VR over conventional training supports further investigation.
11	Park and Park, 2016	n=30 (experimental group15/control group 15)	• Nintendo Wii • Nintendo Wii+MP sessions	• 20 sessions (5 days in a week)	• FMA • BBT • MAL	Game-based virtual reality movement therapy alone may be helpful to improve functional recovery of the upper extremity.
12	Rand et al., 2014	n=29 (experimental group 15/control group 14)	• Video games • Traditional therapy	• 3 months (1-hr session×2 sessions per week)	• The number of repetitions and classified movements as purposeful or nopurposeful using videotapes	Video games elicited more upper extremity purposeful repetitions and higher acceleration of movement compared with traditional therapy.
13	Rand et al., 2017	n=23 (experimental group13/control group 10)	• Video-games • Traditional self-training	• 1-hr/day, 6-times/wk, 5 weeks	• ARAT • MAL • BBT	Upper extremity functional improvement can be achieved by self-training at the chronic stage.
14	Saposnik et al., 2010	n=22 (experimental group 11/control group 11)	• Reality using the Nintendo Wii gaming system • Recreational therapy (playing cards, bingo, or "Jenga")	• 60 min each over a 14-day period • These 8 sessions	• WMFT • BBT • Stroke impact scale	The Wii gaming technology represents a safe, feasible, and potentially effective alternative to facilitate rehabilitation therapy.
15	Saposnik et al., 2016	n=137 (experimental group 67/control group 70)	• Nintendo Wii gaming system (VRWii) • Simple recreational activities (playing cards, bingo, Jenga, or ball game)	• 10 sessions, 60 min	• WMFT	Virtual reality is safe, but showed no significant benefits as an add-on therapy to conventional rehabilitation when compared with recreational activity.
16	Shin et al., 2016	n=46 (experimental group 24/control group 22)	• Smart Glove group • Conventional intervention group	• 20 sessions for 30 min per day of 4 week	• FMA • Jebsen-Taylor hand function test • Purdue pegboard test • Stroke impact scale	VR-based rehabilitation combined with standard occupational therapy might be more effective than amount-matched conventional rehabilitation for improving distal upper extremity function and quality of life.
17	Shin et al., 2015	n=32 (experimental group 16/control group 16)	• VR rehabilitation plus conventional OT • Conventional OT	• 20 sessions over 4 weeks	• SF-36 • Hamilton Depression Rating Scale • FMA	VR rehabilitation has specific effects on health-related quality of life, depression, and upper extremity function.
18	Sin & Lee, 2013	n=40 (experimental group 20/control group 8)	• VR training using Xbox Kinect and conventional occupational therapy • Conventional occupational therapy	• 6 weeks of intervention	• FMA • ROM • BBT	The potential efficacy of Xbox Kinect in the rehabilitation of post-stroke survivors needs to be investigated in greater depth.
19	Stockley et al., 2017	n=12 (YouGrabber group 6/personalized therapeutic exercise group 6)	• YouGrabber VR system: 6 games which focus upon dexterity mirror imaging and grasp and release in different positions • Personalized therapeutic exercise	• 30 min, 18 sessions over 12 weeks	• MAL • BBT • Fatigue Severity Score	The YouGrabber appeared practical and may improve upper limb activities in people several months after stroke.

(*Continued to the next page*)

Table 3. Continued

No.	Study	Patients (n)	Intervention		Outcome measure (primary)	Outcome
			Intervention/groups	Session/time		
20	Subramanian et al., 2013	n=32 (experimental group 20/control group 8)	• VR for poststroke arm motor rehabilitation • Advantages over physical environment training	• 12 sessions over 4 weeks	• FMA • Reaching performance scale for stroke	VR training led to more changes in the mild group and a motor recovery pattern in the moderate-to-severe group indicative of less compensation.
21	Thielbar et al., 2014	n=23 (experimental group 13/control group 10)	• AVK system • intensive dose of occupational therapy	• 18-hr-long sessions of extensive therapy (3 times per week for 6 weeks)	• Jebsen-Taylor hand function test • ARAT • FMA • Grip and pinch strengths	Actively assisted individuation therapy comprised of non-task specific modalities may prove to be valuable clinical tools for increasing the effectiveness and efficiency of therapy following stroke.
22	Türkbey et al., 2017	n=20 (experimental group 10/control group 10)	• Conventional therapy • Experimental group received additional Xbox Kinect training	• 4 weeks (60 min/day, 5 day/week).	• Treatment attendance rate • Patient feedback • Proportion of adverse events • BBS	Xbox Kinect training appears feasible and safe in upper extremity rehabilitation after stroke.
23	Viana et al., 2014	n=22 (experimental group 11/control group 11)	• VR therapy and transcranial direct current stimulation • VR therapy and sham transcranial direct current stimulation	• 15 sessions with 13 min	• FMA • MAS • Grip strength • Specific quality of life scale • Minimal clinically important differences	tDCS, combined with VR therapy, should be investigated and clarified further.
24	Zondervan et al., 2016	n=18 (experimental group 9/control group 9)	• Home-based Music Glove therapy • Conventional tabletop exercises	• 3 hr per week for 3 weeks	• BBT	MusicGlove therapy was not superior to conventional tabletop exercises for the primary end point.
25	Takahashi et al., 2007	n=17 (experimental group 7/control group 6)	• Active assist mode robotic therapy • Active assist non-mode robotic therapy	• 15 daily sessions, on weekdays, over 3 weeks • 1.5 hr per each session	• ARAT • FMA • NIH Stroke Scale • GDS • Nottingham Sensory Assessment • Assessment of apraxia • Grip and pinch strength • Active range of motion • 9-hole Peg test • Stroke Impact Scale • MAS	A robot-based therapy showed improvements in hand motor function after chronic stroke.

ARAT, action research arm test; AVK, actuated virtual keypad; BBS, Berg Balance Scale; BBT, Box and Blocks Test; COPM, Canadian Occupational Performance Measure; EQ-5D, EuroQol-5 Dimension; FMA, Fugl-Meyer Assessment; FRT, Function Reaching Test; GDS, Geriatric Depression Scale; MAL, motor activity log; MAS, Modified Ashworth Scale; ROM, range of motion; SF-36, 36-item short form health survey; rDCS, transcranial direct current stimulation; VR, virtual reality; WMFT, Wolf Motor Function Test.

the assessors was properly addressed in three studies (Ballester et al., 2016; Choi et al., 2014; Shin et al., 2014). Data on all the patients and those who dropped out from the study were handled properly in seven studies (Ballester et al., 2016; Choi et al., 2014; da Silva Cameirão et al., 2011; Kiper et al., 2014; Piron et al., 2010; Shin et al., 2014; Zheng et al., 2015).

The overall effect size was moderate (0.41, $P<0.001$). The 95% CI ranged from 0.25 to 0.57 (Fig. 2). No significant heterogeneity and publication bias were found. Analysis of the funnel plot revealed the nine values that were to be distributed in every section, taking an asymmetric funnel shape, with more values falling on the right side of the mean effect size plot (Fig. 3).

In our test for statistical heterogeneity, a Cochran Q value of 21.78 ($P<0.001$) indicated no significant heterogeneity. The fixed-effects and random-effects models showed effect sizes of 0.41 and 0.65, respectively, providing further evidence of the lack of statistical heterogeneity among the studies included in the present meta-analysis (Tables 4, 5).

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Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Pron et al., 2010	1.039	0.314	0.099	0.423	1.654	3.309	0.001
Cameirao et al., 2011	0.641	0.513	0.263	-0.364	1.645	1.249	0.212
Turolla et al., 2013	0.180	0.113	0.013	-0.041	0.401	1.599	0.110
Choi et al., 2014	2.365	0.583	0.340	1.222	3.507	4.057	0.000
Kiper et al., 2014	0.724	0.312	0.097	0.113	1.334	2.323	0.020
Shin et al., 2014	0.742	0.517	0.267	-0.271	1.755	1.435	0.151
Yin et al., 2014	0.779	0.433	0.187	-0.069	1.628	1.800	0.072
Zheng et al., 2015	0.393	0.191	0.036	0.019	0.767	2.059	0.040
Ballester et al., 2016	0.377	0.319	0.102	-0.249	1.002	1.181	0.238
	0.414	0.081	0.007	0.255	0.572	5.105	0.000

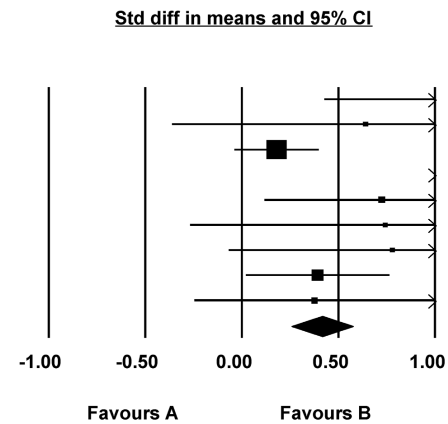

Fig. 2. Forest plot showing individual effect sizes. CI, confidence interval.

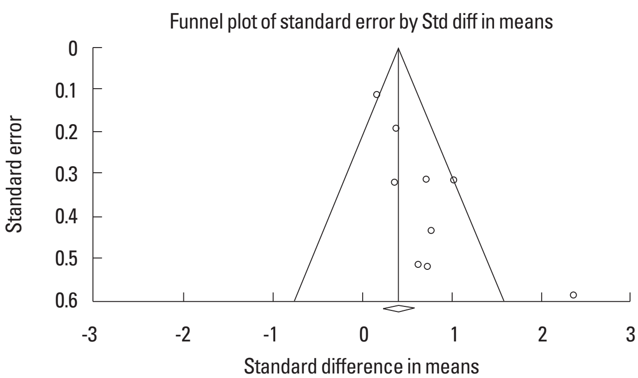

Fig. 3. Funnel plot of publication bias.

DISCUSSION

The present systematic review aimed to summarize interventions and outcome measurements after the use of VR technologies as interventions for improving upper extremity function and independence in performing activities of daily living in stroke survivors. Moreover, the effect of the VR intervention in the stroke patients was assessed in a meta-analysis.

In the 34 studies for systematic review, the assessment tools used for upper extremity functions were FMA, WMFT, and MAL. Meanwhile, the BI and FIM were used to assess for independence. Most of the applied interventions used VR using computer programs, followed by video games and Wii. Nine studies for meta-analysis used independence in activities of daily living as an outcome measure. The overall effect size of applying VR intervention in stroke survivors was 0.41, which is considered statistically significant. This result indicates that VR intervention has a moderate effect on improving upper extremity function and independence in activities of daily living. No significant heterogeneity and publication bias were identified. An adequate effect size was used for each study included in the meta-analysis. It may also have

Table 4. Frequency of virtual reality intervention

Types of intervention	Frequency (%)
Based VR system	
VR by computer	9 (26.5)
Video game	6 (17.6)
Video capture VR	1 (2.9)
VR with bilateral training	1 (2.9)
Goal oriented movement VR	1 (2.9)
Hand/arm training	1 (2.9)
Reinforced feedback in virtual environment	1 (2.9)
Based game	
Wii	4 (11.8)
Xbox Kinect training	2 (5.9)
Based robot	
Wilmington robotic exoskeleton	1 (2.9)
Robotic therapy	1 (2.9)
Etc	
RehabMaster	1 (2.9)
rTMS with VR	1 (2.9)
Smart Glove	1 (2.9)
YouGrabber virtual system	1 (2.9)
Home based music glove therapy	1 (2.9)
Smartphone program	1 (2.9)
Total	34 (100)

VR, virtual reality; rTMS, repetitive transcranial magnetic stimulation.

Table 5. Heterogeneity

Model	Effect size	*P*-value	*Q*-value	*P*-value
Fixed	0.41	<0.001	21.78	<0.001
Random	0.65	<0.001	-	-

affected the results of the overall effect size because only few studies calculated the effect size in a meta-analysis.

In the 34 studies, the time and amount of therapy was similar between the VR-based intervention and control groups. In 18 studies, the participants in the experiment group received a VR-based intervention. Meanwhile, in the control group, the participants underwent the conventional rehabilitation program (Choi et al., 2014; Crosbie et al., 2012; da Silva Cameirão et al., 2011; Housman et al., 2009; Kiper et al., 2014; Lee et al., 2016a; Levin et al., 2012; Piron et al., 2010; Rand et al., 2014; Sin and Lee, 2013; Shin et al., 2014; Shin et al., 2015; Shin et al., 2016; Thielbar et al., 2014; Türkbey et al., 2017; Turolla et al., 2013; Yin et al., 2014; Zheng et al., 2015; Zondervan et al., 2016). In 16 studies, the control group received treatments similar or different from those used in the experiment group (Adie et al., 2017; Ballester et al., 2016; Broeren et al., 2008; Fluet et al., 2014; Kong et al., 2016; Lee et al., 2014; Lee et al., 2016a; Park and Park, 2016; Rand et al., 2017; Saposnik et al., 2010; Saposnik et al., 2016; Stockley et al., 2017; Subramanian et al., 2013; Viana et al., 2014; Zheng et al., 2015).

The results of this systematic review showed that VR intervention was more effective than the conventional therapy, as suggested by the significant improvements in upper limb function and independence in activities of daily living. For the assessment of upper extremity functions, FMA, WMFT, and MAL were commonly used, and BI and FIM were the most frequently used assessment tools for elucidating the effect of VR intervention on independence in activities of daily living. Although various VR-based rehabilitative interventions have been used in stroke patients, their efficacy in improving upper extremity function and independence in performing activities of daily living has not been fully elucidated. This study is unique because it examined upper extremity function and independence in performing activities of daily living. Our results showed that VR interventions may be effective for improving upper limb function and independence in performing activities of daily living in stroke patients.

In this study, only published articles obtained from the search process were reviewed, which may be a limitation because unpublished data and review papers or reports were excluded. Therefore, further studies that include a broader search for literatures on school-aged children must be conducted. Nevertheless, this study suggests various intervention methods that promote the development of cognitive function among children in the developmental stages. The cognitive function during the early stage of development is essential for the performance of children. Various cognitive approaches to rehabilitation therapy should be considered because it is an important skill in the preparation for learning (Cicerone et al., 2005). Furthermore, movements practiced in a virtual environment that closely mimic real-world tasks have been shown to maximize the effects of training (Chen et al., 2016; Laver et al., 2012). On the basis of previous studies, we investigated how VR intervention similar to real-world interventions affects upper limb function and independence in performing activities of daily living in stroke patients (da Silva Cameirão et al., 2011; Kiper et al., 2014; Shin et al., 2016). Training using intensive VR-based intervention has improved both upper and lower extremity functions and independence in performing activities of daily living in both the chronic and subacute populations (Chen et al., 2016; Lee et al., 2016b; Shin et al., 2016).

We cannot conclude whether VR-based interventions are more effective in promoting the recovery of independence in activities of daily living after stroke than any other approaches owing to the limited evidence from the meta-analysis. Nine studies for meta-analysis used variable VR-based intervention programs such as computer-, cellphone-, game-, and VR-based rehabilitation programs (Ballester et al., 2016; Choi et al., 2014; da Silva Cameirão et al., 2011; Kiper et al., 2014; Lee et al., 2016a; Piron et al., 2010; Shin et al., 2014; Turolla et al., 2013; Zheng et al., 2015). Moreover, the studies used various clinical measurement tools and were subject to methodological flaws. We suggest that these intervention factors affected the analysis of qualitative effects in this study. We also recommend that future studies should concentrate on investigating the effectiveness of clearly described individual techniques based on therapeutic methodology. For example, previous studies used small sample sizes; failed to include randomized controlled trials for experimenter bias, equivalence of participants, and co-interventions; and used poorly defined treatments and inappropriate outcome measures. The number of large-scale, multicenter randomized controlled trials that offer rehabilitative clinicians and stroke survivors a higher level of reliability is limited. Therefore, the important conclusions that can be drawn from these VR-based intervention studies are that collectively, we try to prove the consistent evidence of the beneficial effects of VR-based therapeutic interventions in comparison with those of other rehabilitation programs.

Finally, VR interventions may be beneficial to stroke patients, and we present the basis for the VR intervention applied in stroke patients by analyzing the intervention methods and type of outcome measurement. The number of VR interventions used in stroke patients may be significant. The study results can be used as a basis for the application of VR interventions in stroke patients

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in clinical settings.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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