# Virtual reality-based rehabilitation in patients following total knee arthroplasty: a systematic review and meta-analysis of randomized controlled trials

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### Abstract

**Background:** Physical therapy is regarded as an essential aspect in achieving optimal outcomes following total knee arthroplasty (TKA). The coronavirus disease 2019 (COVID-19) pandemic has made face-to-face rehabilitation inaccessible. Virtual reality (VR) is increasingly regarded as a potentially effective option for offering health care interventions. This systematic review and metaanalysis investigate VR-based rehabilitation's effectiveness on outcomes following TKA.

**Methods:** From inception to May 22, 2021, PubMed/Medline, Embase, Web of Science, the Cochrane Central Register of Controlled Trials, Scopus, PsycINFO, Physiotherapy Evidence Database, China National Knowledge Infrastructure, and Wanfang were comprehensively searched to identify randomized controlled trials (RCTs) evaluating the effect of VR-based rehabilitation on patients following TKA according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement and the Cochrane Handbook for Systematic Reviews of Interventions.

**Results:** Eight studies were included in the systematic review, and seven studies were included in the meta-analysis. VR-based rehabilitation significantly improved visual analog scale (VAS) scores within 1 month (standardized mean difference [SMD]: -0.44; 95% confidence interval [CI]: -0.79 to -0.08, P = 0.02), the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) within 1 month (SMD: -0.71; 95% CI: -1.03 to -0.40, P < 0.01), and the Hospital for Special Surgery Knee Score (HSS) within 1 month and between 2 months and 3 months (MD: 7.62; 95% CI: 5.77 to 9.47, P < 0.01; MD: 10.15; 95% CI: 8.03 to 12.27, P < 0.01; respectively) following TKA compared to conventional rehabilitation. No significant difference was found in terms of the Timed Up and Go (TUG) test.

**Conclusions:** VR-based rehabilitation improved pain and function but not postural control following TKA compared to conventional rehabilitation. More high-quality RCTs are needed to prove the advantage of VR-based rehabilitation. As the COVID-19 pandemic continues, it is necessary to promote this rehabilitation model.

Keywords: Arthroplasty, Replacement, Knee; Virtual Reality; Virtual Reality Exposure Therapy; Rehabilitation; Systematic review; Meta-analysis

## Introduction

Total knee arthroplasty (TKA) is one of the most common surgeries for patients suffering from end-stage osteoarthritis.<sup>[1]</sup> Although significant advancements have been achieved in implant design, surgical techniques, and anesthetic modalities, patient satisfaction and perception of success following TKA are relatively low.<sup>[2,3]</sup> Approximately 20% of patients are dissatisfied with their TKA outcomes.<sup>[4]</sup> Although various programs of post-operative rehabilitation exist worldwide, physiotherapy is regarded as an essential component in achieving optimal outcomes following TKA.<sup>[5]</sup> Post-operative progressive exercise program achieves faster recovery, better function, and improved range of motion (ROM).<sup>[6]</sup>

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The post-operative rehabilitation program following TKA has mainly shifted toward outpatient and community over the past decade in the United States.<sup>[7]</sup> In addition, the coronavirus disease 2019 (COVID-19) pandemic has had a profound impact on the health care system.<sup>[8]</sup> Face-to-face post-operative rehabilitation has become inaccessible during the pandemic, which has led to the rapid development of contactless methods of rehabilitation.<sup>[9]</sup> By delivering medical care at a distance, telehealth and virtual reality (VR) are increasingly regarded as potentially effective health-care interventions.<sup>[10]</sup> By using various auxiliary devices, VR provides interactive computer environments or games that are similar to real-world experiences.<sup>[11]</sup> VR-based rehabilitation results in excellent outcomes for patients due to its ability to provide simulations of real

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environments.<sup>[12]</sup> The effectiveness of VR-based rehabilitation has been verified in Parkinson disease, stroke, and cerebral palsy.<sup>[11,13,14]</sup> In orthopedic rehabilitation, the advantage of VR-based rehabilitation has been explored in patients with osteoarthritis, low back pain, and anterior cruciate ligament injury.<sup>[6,15,16]</sup> Although some studies have investigated the effect of VR equipment on TKA patients,<sup>[17,18]</sup> there is insufficient evidence to demonstrate the advantage of VR. A systematic review reported that VRbased rehabilitation has no benefit in increasing function, relieving pain, or increasing satisfaction following TKA compared to conventional rehabilitation.<sup>[19]</sup> However, Blasco *et al*<sup>[19]</sup> included a limited number of trials from a few databases, which makes the meta-analysis impossible. Recently, some randomized controlled trials (RCTs) detected the effect of VR-based rehabilitation on TKA outcomes.<sup>[20,21]</sup> To our knowledge, this is a rare metaanalysis assessing the effect of VR-based rehabilitation programs on the outcomes of patients following TKA surgeries. Therefore, this systematic review and metaanalysis investigates VR-based rehabilitation's effectiveness on TKA outcomes.

# **Methods**

All analyses were based on data from previously published literature. Thus, neither ethical approval nor patient consent was required. This systematic review and metaanalysis were performed following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement<sup>[22]</sup> and the Cochrane Handbook for Systematic Reviews of Intervention.<sup>[23]</sup> Our study was registered on PROSPERO, with registration number CRD42021258778.

## Search strategy

From inception to May 22, 2021, the following databases were comprehensively searched by two independent reviewers to identify potentially relevant studies: PubMed/Medline, Embase, Web of Science, the Cochrane Central Register of Controlled Trials, Scopus, PsycINFO, Physiotherapy Evidence Database (PEDro), Cumulative Index to Nursing and Allied Health Literature, China National Knowledge Infrastructure, and Wanfang. In addition, related studies were manually searched to obtain relevant articles. The search was performed using a combination of the following search terms on May 22, 2021: (total knee arthroplasty OR total knee replacement) AND (VR OR VR exposure therapy OR game(s) OR computer game(s) OR videogame(s) OR video game(s) OR active game(s) OR serious game(s) OR exergam OR interactive OR immersive OR Wii OR Kinect OR Xbox OR PlayStation). The search strategies for each database are presented in Supplementary file, http://links.lww.com/ CM9/A822. In addition, the reference lists of the publications identified from the electronic databases were searched manually for additional relevant articles.

# Inclusion and exclusion criteria

The selection of literature was based on the following inclusion criteria:

Population: adult patients who had undergone TKA surgery.

Intervention: VR-based rehabilitation.

Comparison: conventional rehabilitation or exercise therapy or other non-VR interventions.

# Outcome

The primary outcomes were the following: visual analog scale (VAS), numerical pain rating scale (NPRS), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Hospital for Special Surgery Knee Score (HSS), Berg Balance Scale (BBS), Timed Up and Go (TUG) test, ROM, Short Form Health Survey-36 (SF-36), and EuroQol Five-Dimensional Questionnaire (EQ-5D).

Type of design: RCTs. No restrictions were made on the publication date or language.

# Exclusion criteria

Trials that included non-TKA patients in the population were excluded. Retrospective studies, non-RCTs, reviews, letters, comments, case reports, conference records, books, protocols, and studies without extractable data were excluded from our meta-analysis.

# Study selection

After removing duplicates, two reviewers independently screened the titles, abstracts, and full texts of the identified studies. When one reviewer identified a study as potentially eligible, the full text was obtained and checked. Disagreements were resolved via discussion with a senior reviewer.

## **Data extraction**

The data extractions were conducted independently by two authors. Disagreements concerning the extracted data were resolved via discussion with a third reviewer. We contacted the first and corresponding authors for any missing details if any important parameters were unavailable. All the extracted data were imported into Excel 2016 (Microsoft Corporation, Redmond, WA, USA) for processing. The following data were collected from each study: (1) the characteristics of each included study, including first author, year of publication, country, study design, number of patients, age, sex, and body mass index; (2) characteristics of the intervention and control groups, including the type of intervention, type of control, and frequency and duration of the rehabilitation program; and (3) outcomes, including the VAS, the NPRS, the WOMAC, the HSS, the BBS, the TUG, ROM, the SF-36, and the EQ-5D.

## Methodological quality assessment

Quality assessments were calculated using the PEDro scale, which includes 11 criteria.<sup>[24]</sup> Each criterion was scored as yes (1 point), no (0 points), or don't know (0 points). The first criteria (eligibility criterion) did not count the total score. Thus, the total score of PEDro ranges from 0 to 10.<sup>[25]</sup> A higher total score indicates higher methodological quality of the clinical study. Studies with a score  $\geq 6$  points

were regarded as "good quality" and a score  $\leq 5$  points as "poor quality."<sup>[26]</sup> We excluded the studies that had a poor quality from this research. The quality assessments were evaluated by two independent reviewers. Disagreements concerning the methodological quality were resolved via discussion with senior reviewers.

#### Statistical analysis

Cochrane Collaboration Review Manager software (RevManVersion 5.3, Oxford, UK) was used to perform the meta-analyses and produce forest plots. Because all the included outcomes were continuous variables in our study, the mean difference (MD) with 95% confidence interval (CI) was used to calculate the total effect of VR-based rehabilitation. If some studies comprised outcomes that were expressed as different measurement methods, units, or grading systems, the standardized MD (SMD) was used to calculate the total effect. The  $I^2$  statistic was used to assess heterogeneity.<sup>[27]</sup> A random-effects model was used when substantial heterogeneity existed (P < 0.05 or  $I^2 > 50\%$ ); otherwise, a fixed-effects model was used. All the results are shown with forest plots. A *P* value < 0.05 demonstrated a statistically significant difference.

#### **Results**

## Study selection

The flowchart of study selection according to PRISMA guidelines was clearly shown in Figure 1. The initial search yielded 547 articles. After removing 247 duplicated

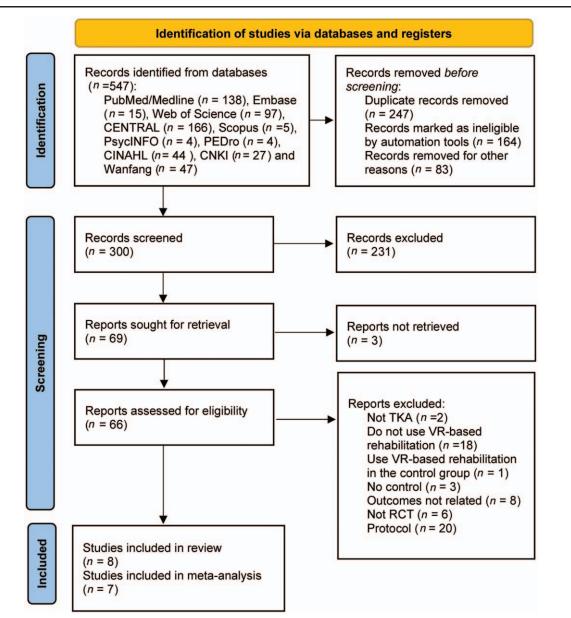


Figure 1: Flow chart of study selection according to PRISMA guidelines. CENTRAL: Cochrane central register of controlled trials; CNKI: China national knowledge infrastructure; EMBASE: Excerpta medica database; PRISMA: Preferred reporting items for systematic reviews and meta-analyses; PEDro: Physiotherapy evidence database; RCT: Randomized controlled trial; TKA: Total knee arthroplasty; VR: Virtual reality.

studies, 300 articles that potentially investigated VR-based rehabilitation on TKA patients were screened. After screening the titles, abstracts, and full texts of the identified studies, eight studies<sup>[17,18,20,21,28-31]</sup> were included in the systematic review, and seven studies<sup>[18,20,21,28-31]</sup> were included in the meta-analysis according to the Cochrane Handbook for Systematic Reviews of Interventions.<sup>[23]</sup>

#### Study characteristics

The eight eligible RCTs enrolled 805 patients following TKA with 408 receiving VR-based rehabilitation and 397 receiving conventional rehabilitation. All included trials were RCTs. The characteristics of the included studies were presented in Table 1. The eight RCTs were conducted in different countries: one in Canada,<sup>[17]</sup> one in Spain,<sup>[18]</sup> two in China,<sup>[28,29]</sup> one in Germany,<sup>[30]</sup> one in Italy,<sup>[20]</sup> one in the USA,<sup>[21]</sup> and one in Korea [Table 1].<sup>[31]</sup> Five of the eight articles were registered before the trials.<sup>[17,18,20,21,30]</sup>

#### Methodological quality

Each included study received a score on the PEDro scale  $\geq 6$  points (range 6–8), which indicated that the methodological quality was "good."<sup>[26]</sup> Owing to the particularity of rehabilitation therapy, it is impossible to blind the participants or therapists. Therefore, blinded participants and therapists were not implemented in all studies. Only two studies achieved concealed allocation.<sup>[20,31]</sup> Three studies failed to blind assessors who measured the outcomes.<sup>[21,29,30]</sup> One study did not provide enough point measures.<sup>[17]</sup> The PEDro scales of the included studies were presented in Table 2.

#### Interventions

The included studies utilized different intervention programs. In Fung et al<sup>[17]</sup>, patients in VR-based rehabilitation received 15 minutes of Nintendo Wii Fit (Nintendo of America, Redmond, WA, USA) gaming activity. The Nintendo Wii included a balance board that provided feedback on exercises performed or games played on the accompanying software.<sup>[17]</sup> Piqueras *et al*<sup>[18]</sup> used an interactive virtual telerehabilitation kit in their study, which was comprised of three parts: wireless sensors, interactive patient application, and a Web portal for the therapist. Patients in the intervention group exercised with this interactive VR for 1 hour a day.<sup>[18]</sup> Jin *et al*<sup>[28]</sup> used VR equipment (Mide Technology Inc., Cangzhou, China) in the intervention group following the second day of TKA. Patients were taught to row a boat in an immersive virtual environment for 30 minutes, three times a day.<sup>[28]</sup> The same VR device was used by Li *et al*<sup>[29]</sup> in another hospital in China.<sup>[29]</sup> Immersive VR of water rowing was conducted for 30 minutes, three times a day in the intervention group. In the study of Eichler *et al*<sup>[30]</sup>, patients in the intervention group used an avatar and real-time visual feedback via a Kinect sensor. The therapist accessed the training frequency and the exercise evaluations by a working portal for training supervision. Gianola et al<sup>[20]</sup> developed a set of VR-based rehabilitation programs for 60 minutes per day in the intervention group. Patients in the control group received similar exercises without VR support. Bettger *et al*<sup>[21]</sup> used the virtual exercise rehabilitation assistant system (VERA, Reflexion Health, San Diego, CA, USA) in their study. Patients in the intervention group exercised with VERA, whereas the patients in the control group exercised following the care team's recommendations.<sup>[21]</sup> Yoon and Son<sup>[31]</sup> used VR glasses (Hyundai Chemistry, South Korea) and a smartphone-based balance game (BASEjump VR: Wingsuit, Gregory, Street Studios, UK) in their study. Patients in the intervention group tried to reach a target whereas avoiding obstacles in the VR environment.<sup>[31]</sup>

## Efficacy outcomes

## Pain

Three studies reported changes in pain on the VAS.<sup>[21,28,29]</sup> One trial used a scale of 0-100 points to score pain.<sup>[20]</sup> Another study measured the difference from baseline using a 0–10 points scale.<sup>[18]</sup> Fung *et al*<sup>[17]</sup> calculated pain grades on a scale of 0-10 points NPRS, which is similar to the VAS.<sup>[32]</sup> However, they only reported the percentage change from baseline without any measures of variability, such as standard deviations. Therefore, it was not easy to include in the meta-analysis. Different measurement units were adopted among the studies, so the SMD calculated the total effect. Our pooled analysis of four articles<sup>[18,20,28,29]</sup> involving 360 participants indicated that VR-based rehabilitation improved pain following TKA, as measured on the VAS, within 1 month compared to the control group (SMD: -0.44; 95% CI: -0.79 to -0.08,  $P = 0.0\overline{2}$ ). Significant heterogeneity between the articles was observed (P = 0.04;  $I^2 = 63\%$ ). However, VRbased rehabilitation could not improve pain between 2 months and 3 months (SMD: -0.35; 95% CI: -1.02 to 0.32, P = 0.31). There was significant heterogeneity between the groups (P < 0.01;  $I^2 = 91\%$ ) [Figure 2].

## WOMAC

Four studies assessed outcomes of the WOMAC.<sup>[20,28,30,31]</sup> Jin *et al*<sup>[28]</sup> estimated WOMAC scores at 1 month, 3 months, and 6 months. Eichler *et al*<sup>[30]</sup> evaluated WOMAC scores at 3 months. Gianola *et al*<sup>[20]</sup> assessed the effect of early VR-based rehabilitation on WOMAC scores at 10 days. Yoon and Son<sup>[31]</sup> utilized full immersion VR-based rehabilitation and measured the WOMAC at 4 weeks. The WOMAC consists of 24 questions that assess areas, such as pain, stiffness, and daily activities. There are a few possible score ranges including 0-240 (derived from the VAS 0-10 or NRS scale), 0–2400 (derived from the VAS 0–100), and 0–96 (derived from a 0–4 Likert scale).<sup>[33]</sup> Three studies<sup>[28,30,31]</sup> used the 0-96 points scale, whereas another<sup>[20]</sup> chose the 0-2400 points scale. Thus, the SMD calculated the total effect. The pooled analysis of WOMAC scores showed that VR-based rehabilitation significantly improved WOMAC scores within 1 month compared to the control group (SMD: -0.71; 95% CI: -1.03 to -0.40, P < 0.01). No significant heterogeneity was found among the groups  $(P = 0.76; I^2 = 0\%)$ . VR-based rehabilitation did not

ladie 1: characteristics of studies included in the meta-analysis adout		virtual reality-dased rehadilitation on total knee artifroplasiy	ni oli lolai kiice arliropia			
Author(s)/year/Country/design/patients (I: C)	Age (years) I: C	Intervention group	Control group	Other rehabilitation in both groups	Functional, balance, gait, and pain outcomes	PEDro score
Fung <i>et al</i> <sup>[17]</sup> /2012/Canada/RCT/27:23	I: 67.9 ± 9.5; C: 68.2 ± 12.8	Exercise with Nintendo Wii Fit games (15 min)	Lower extremity exercises (15 min)	Physiotherapy session	2MWT, ROM, timed standing, LOR, ABCS, 1 EFS NIDBS of 2 modes	9
Piqueras <i>et al</i> <sup>[18]</sup> /2013/Spain/RCT/68: 65	1+C: 73.3 ± 6.5	Exercise with interactive VR (1 h/day, 3 m)	Standard rehabilitation (1 h/ day, 3 m)	Inpatient care, outpatient intervention, and conventional physical therapy	Active knee extension and active knee extension and active knee flexion; quadriceps muscle strength; hamstring muscle strength; timed get-up and go test, VAS, WOMAC, ROM at 10 days and 3	М
Jin <i>et a</i> / <sup>128]</sup> /2018/China/RCT/33:33	I: 66.45 ± 3.49; C: 66.30 ± 4.41	Row a boat using knee flexion (interaction of VR) (30 min, 3 times/day)	Flex knees passively using their arms for 20 s followed by relaxing for 40 s (30 times/set, 3 sets/	Foot dorsiflexion and plantar flexion beginning; Passive knee	WOMAC at 1, 3, 6 months; WOMAC at 1, 3, 6 months; HSS at 1, 3, 6, 7 days; ROM 3, 7, 14 days;	М
Li et al <sup>(29)</sup> /2018/China/RCT/39:39	I: 71. 82 ± 7. 98; C: 72. 97 ± 7. 82	Row a boat in an immersive VR of water rowing (30 min, 3 times/ day, 2	CPM (20 min, 2 times/ day, 2 weeks)	None	VAS at 2 weeks, 2 months; HSS at 2 weeks, 2 months; BBS at 2 weeks, 2	9
Eichler <i>et a</i> l <sup>130]</sup> /201 <i>9</i> /Germany/RCT/48:39	I: 53.3 ± 7.0; C: 56.8 ± 5.7	Exercise following the screen by an avatar and real-time visual feedback by a Kinect sensor (individualized number of sets and repetitions, and the duration, 3 times/ wwek 3 months)	None	3 weeks inpatient rehabilitation; multimodal intensified program; Physiotherapy;	6MWT, stair ascend test, TUG test, five times chair rise test, SF-36, WOMAC at 3 months;	Q
Gianola <i>et al</i> <sup>[20]</sup> /2020/Italy/RCT/35: 39	1: 66.6±8.7; C: 70.7±8.5	Exercises for monutory rehabilitation (60 min/day, 1 week)	Similar exercises without VR support (60 min/ day, 1 week)	CPM and functional exercises (60 min/ day, at	VAS, WOMAC, EQ-5D, GPE, FIM, ROM at 10 days,	×
Bettger <i>et af<sup>(21)</sup></i> /2020/USA/RCT/143: 144	I: 65.4 ± 7.7; C:65.1 ± 9.2	Exercise with VR equipment (individualized the frequency and duration of use were unrestricted)	Exercise followed their care team's recommendations	6-week clinic visit and reexamine	VAS at 6 weeks KOOS at 6, 12 weeks ROM at 6 weeks 10 m gait speed at 6	9
Yoon et af <sup>[31]</sup> /2020/Korea/RCT/15:15	I: 72.26 ± 36.5; C:71.86 ± 4.89	Train with the VR application wearing VR glasses (20 min/ day, 5 days/ week, 2weeks)	None	CPM (30 min/ day, 5 times/week, 23 days); Exercise therapy (30 min/ day, 5 times/ week, 2 weeks)	TUG, WOMAC at 4 weeks	×
<sup>2</sup> MWT: 2 minute walk test; 6MWT: 6 minute walk test; ABCS: Activity-specific balance confidence scale; BBS: Berg balance scale; C: Control; CPM: Conventional continuous passive motion; EQ-5D: EuroQol five-dimensional questionnaice; FIM: Functional independent measure; GPE: Global perceived effect; HSS: Hospital for Special Surgery Knee score; I: Intervention; KOOS: Knee injury and osteoarthritis outcome score; LEFS: Lower extremity functional scale; JOR: Length of outpatient rehabilitation; NPRS: Numeric pain rating scale; PEDro: Physiotherapy evidence database; RCT: Randomized controlled trial; ROM: range of motion; SF-36: Short form health survey-36; TUG: Timed up and go test; VAS: Visual analogue scale; VR: Virtual reality; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index.	nute walk test; ABCS: Activity-specific H nctional independent measure; GPE: G inctional scale; LOR: Length of outpat ort form health survey-36; TUG: Time	balance confidence scale; BBS: Ber Jlobal perceived effect; HSS: Hos tient rehabilitation; NPRS: Nume ed up and go test; VAS: Visual a	g balance scale; C: Control; pital for Special Surgery K ric pain rating scale; PEDro nalogue scale; VR: Virtual	CPM: Conventional con nee score; I: Intervention : Physiotherapy evidencc reality; WOMAC: Wes	tinuous passive motion; EQ-5D: 1 1; KOOS: Knee injury and osteo e database; RCT: Randomized co tern Ontario and McMaster Un	EuroQol arthritis ontrolled iversities

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#### Table 2: Methodological quality assessment by PEDro scales.

Studies	Eligibility criteria	Random allocation	Concealed allocation	Baseline comparison	Blinded participates	Blinded therapists	Blinded assessors	Outcomes obtained	Intention- to-treat	Between- group comparisons	Point measures and variability	Total score
Fung et al <sup>[17]</sup> , 2012	YES	YES	NO	YES	NO	NO	YES	YES	YES	YES	NO	6
Piqueras <i>et al</i> <sup>[18]</sup> , 2013	YES	YES	NO	YES	NO	NO	YES	YES	YES	YES	YES	7
Jin et al <sup>[28]</sup> , 2018	YES	YES	NO	YES	NO	NO	YES	YES	YES	YES	YES	7
Li et al <sup>[29]</sup> , 2018	YES	YES	NO	YES	NO	NO	NO	YES	YES	YES	YES	6
Eichler <i>et al</i> <sup>[30]</sup> , 2019	YES	YES	NO	YES	NO	NO	NO	YES	YES	YES	YES	6
Gianola <i>et al</i> <sup>[20]</sup> , 2020	YES	YES	YES	YES	NO	NO	YES	YES	YES	YES	YES	8
Bettger et al <sup>[21]</sup> , 2020	YES	YES	NO	YES	NO	NO	NO	YES	YES	YES	YES	6
Yoon and Son <sup>[31]</sup> , 2020	YES	YES	YES	YES	NO	NO	YES	YES	YES	YES	YES	8

PEDro: Physiotherapy evidence database.

	Expe	erimen	tal	C	ontrol		1	Std. Mean Difference		Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV. Random, 95% CI	Year	IV. Random. 95% CI
2.1.1 within 1 m										
Piqueras 2013	-0.69	1.44	72	-0.61	1.87	70	15.3%	-0.05 [-0.38, 0.28]	2013	
Jin 2018	3.87	0.55	33	4.42	0.79	33	12.8%	-0.80 [-1.30, -0.30]	2018	
Li 2018	2.54	0.69	39	3.1	0.96	39	13.5%	-0.66 [-1.12, -0.21]	2018	
Gianola 2020	24.62	16.8	35	31.23	19.59	39	13.5%	-0.36 [-0.82, 0.10]	2020	
Subtotal (95% CI)			179			181	55.2%	-0.44 [-0.79, -0.08]		
Heterogeneity: Tau <sup>2</sup> =	0.08; Ch	ni <sup>2</sup> = 8.0	07, df =	3 (P =	0.04); l <sup>2</sup>	= 63%	1	in the second second		
Test for overall effect:	Z = 2.42	(P = 0	.02)	0.5						
2.1.2 2 to 3 m										
Piqueras 2013	-1.79	2.45	68	-2.3	2.03	65	15.2%	0.22 [-0.12, 0.57]	2013	
Li 2018	1.62	0.54	39	2.51	0.86	39	13.1%	-1.23 [-1.71, -0.74]	2018	
Bettger 2020	2.7	2	143	3	2.6	144	16.6%	-0.13 [-0.36, 0.10]	2020	
Subtotal (95% CI)			250			248	44.8%	-0.35 [-1.02, 0.32]		
Heterogeneity: Tau <sup>2</sup> =	0.32; Ch	$i^2 = 23$	.45, df	= 2 (P <	0.0000	)1);   <sup>2</sup> =	91%			
Test for overall effect:	Z = 1.02	(P=0	.31)	COLUMN TO A COLUMN		1997				
		1								
Total (95% CI)			429			429	100.0%	-0.40 [-0.73, -0.06]		
Heterogeneity: Tau <sup>2</sup> =	0.16; Ch	ni² = 33	.39, df	= 6 (P <	0.0000	)1);   <sup>2</sup> =	82%			
Test for overall effect:	Z = 2.30	(P = 0	.02)							-1 -0.5 0 0.5 1 Favours [experimental] Favours [control]

Figure 2: Forest plots of the meta-analysis of the effect of VR-based rehabilitation vs. conventional rehabilitation on VAS scores. Cl: Confidence interval; VR: Virtual reality; VAS: Visual analog scale; SD: Standard deviation.

improve WOMAC scores at 3 months (SMD: -0.46; 95% CI: -1.05 to 0.13, P = 0.12). However, there was significant heterogeneity between the groups (P = 0.07;  $I^2 = 69\%$ ). Only one study<sup>[28]</sup> reported WOMAC scores at 6 months, and the subgroup analysis showed that VR-based rehabilitation improved WOMAC scores (SMD: -1.17; 95% CI: -1.69 to -0.64, P < 0.01). Heterogeneity was not applicable in this subgroup [Figure 3].

## HSS

Two RCTs reported changes in the HSS.<sup>[28,29]</sup> Jin *et al*<sup>[28]</sup> estimated the HSS at 1 month, 3 months, and 6 months, whereas Li *et al*<sup>[29]</sup> evaluated the HSS at 2 weeks and 2 months. Given that HSS was measured with the same units in both studies, the MD calculated the total effect. Our pooled analysis shows that VR-based rehabilitation significantly improved the HSS within 1 month compared to the control group (MD: 7.62; 95% CI: 5.77 to 9.47, P < 0.01). There was no significant heterogeneity in the group analysis (P = 0.56;  $I^2 = 0\%$ ). In addition, VR-based rehabilitation improved the HSS between 2 months and 3 months (MD: 10.15; 95% CI: 8.03 to 12.27, P < 0.01). No significant heterogeneity was detected (P = 0.55;  $I^2 = 0\%$ ). One study<sup>[28]</sup> reported the HSS at 6 months

and found that VR-based rehabilitation improved the HSS (MD: 7.16; 95% CI: 5.07 to 9.25, P < 0.01). Heterogeneity was not applicable in this subgroup [Figure 4].

## TUG

Two studies reported changes in TUG scores.<sup>[31]</sup> Piqueras *et al*<sup>[18]</sup> assessed differences of TUG scores from baseline to 10 days and 3 months.<sup>[18]</sup> Yoon and Son<sup>[31]</sup> recorded TUG scores at 4 weeks. Since both studies used different methods of recording, we used the SMD to measure the total effect. The pooled analysis showed that VR-based rehabilitation could not significantly improve the TUG score within 1 month nor 3 months (SMD: -0.98; 95% CI: -2.02 to 0.06, P = 0.06; SMD: 0.27; 95% CI: -0.23 to 0.76, P = 0.29, respectively). The two subgroups showed high heterogeneity between the articles (P = 0.01,  $I^2 = 85\%$ ; P = 0.07,  $I^2 = 70\%$ , respectively) [Figure 5].

#### BBS

Only one study reported the BBS score. Li *et al*<sup>[29]</sup> found that VR-based rehabilitation improved the BBS score at 2 weeks and 2 months compared to conventional continuous passive motion (CPM) rehabilitation (29.31  $\pm$  4.64 *vs*.

	Exp	erimenta	al	(	Control		S	Std. Mean Difference		Std. Mean Difference			
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV. Random. 95% CI	Year	IV. Random, 95% CI			
1.1.1 within 1 m													
Jin 2018	32	5.24	33	35.06	5.19	33	17.5%	-0.58 [-1.07, -0.09]	2018				
Gianola 2020	729.57	175.73	35	904.48	229.14	39	18.1%	-0.84 [-1.32, -0.36]	2020				
Yoon 2020	32.8	3.91	15	35.87	4.47	15	10.6%	-0.71 [-1.45, 0.03]	2020				
Subtotal (95% CI)			83			87	46.2%	-0.71 [-1.03, -0.40]		◆			
Heterogeneity: Tau <sup>2</sup> =	0.00; Chi	<sup>2</sup> = 0.56,	df = 2 (	P = 0.76	); $I^2 = 0\%$	6				(			
Test for overall effect:	Z = 4.50	(P < 0.00	001)										
1.1.2 3 m													
Jin 2018	25.79	4.2	33	29.67	5.55	33	17.2%	-0.78 [-1.28, -0.28]	2018				
Eichler 2019	11.5	12.7	48	13.9	14.3	39	20.2%	-0.18 [-0.60, 0.25]					
Subtotal (95% CI)			81			72	37.4%	-0.46 [-1.05, 0.13]					
Heterogeneity: Tau <sup>2</sup> =	0.13; Chi	<sup>2</sup> = 3.23,	df = 1 (	P = 0.07	); l <sup>2</sup> = 69	%							
Test for overall effect:	Z = 1.54	(P = 0.12	:)	10.000									
1.1.3 6 m													
Jin 2018	21.58	4.19	33	26.33	3.85	33	16.4%	-1.17 [-1.69, -0.64]	2018				
Subtotal (95% CI)			33			33	16.4%	-1.17 [-1.69, -0.64]					
Heterogeneity: Not ap	plicable												
Test for overall effect:	Z = 4.36	(P < 0.00	01)										
Total (95% CI)			197			192	100.0%	-0.69 [-0.98, -0.40]		•			
Heterogeneity: Tau <sup>2</sup> =	0.06; Chi	$^{2} = 9.47$	df = 5 (	P = 0.09	); $ ^2 = 47^{\circ}$	%			-				
Test for overall effect:				1 James	1011-105					-2 -1 0 1 2			
Test for subaroup diffe		a second second second		2(P = 0)	19), $ ^2 = 4$	10.6%				Favours [experimental] Favours [control]			

Figure 3: Forest plots of the meta-analysis of the effect of VR-based rehabilitation vs. conventional rehabilitation on WOMAC scores. CI: Confidence interval; VR: Virtual reality; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index; SD: Standard deviation; m: month.

	Exp	eriment	tal	C	ontrol			Mean Difference		Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV. Random, 95% CI	Year	IV. Random, 95% CI
4.1.1 within 1 m										
Jin 2018	68.39	4.32	33	60.45	4.56	33	27.5%	7.94 [5.80, 10.08]	2018	
Li 2018	76	8.64	39	69.31	7.76	39	12.1%	6.69 [3.05, 10.33]	2018	
Subtotal (95% CI)			72			72	39.6%	7.62 [5.77, 9.47]		•
Heterogeneity: Tau <sup>2</sup> =	0.00; Ch	$hi^2 = 0.3$	4, df =	1(P = 0)	).56); I	<sup>2</sup> = 0%				
Test for overall effect:	Z = 8.08	(P < 0.	00001)							
4.1.2 2 to 3 m										
Jin 2018	77.73	5.48	33	67.94	4.51	33	23.2%	9.79 [7.37, 12.21]	2018	
Li 2018	89.63	10.69	39	78.31	8.88	39	8.9%	11.32 [6.96, 15.68]	2018	
Subtotal (95% CI)			72			72	32.1%	10.15 [8.03, 12.27]		•
Heterogeneity: Tau <sup>2</sup> =	0.00; Ch	$hi^2 = 0.3$	6, df =	1(P = 0)	).55); I	$^{2} = 0\%$				
Test for overall effect:										
4.1.3 6 m										
Jin 2018	87.55	4.29	33	80.39	4.39	33	28.3%	7.16 [5.07, 9.25]	2018	
Subtotal (95% CI)			33			33	28.3%	7.16 [5.07, 9.25]		•
Heterogeneity: Not ap	plicable									
Test for overall effect:	Z = 6.70	(P < 0.	00001)							
Total (95% CI)			177			177	100.0%	8.30 [6.92, 9.67]		•
Heterogeneity: Tau <sup>2</sup> =	0.60; Ch	$hi^2 = 5.2$	8, df =	4 (P = 0	).26); I	2 = 24%	0			
Test for overall effect:										-10 -5 0 5 10
Test for subaroup diffe		Succession 1			= 0.10	$ ^2 = 5$	6.4%			Favours [experimental] Favours [control]

Figure 4: Forest plots of the meta-analysis of the effect of VR-based rehabilitation vs. conventional rehabilitation on HSS scores. Cl: Confidence interval; HSS: Hospital for Special Surgery Knee Score; VR: Virtual reality; SD: Standard deviation; m: month.

 $24.20 \pm 3.84$ , P = 0.00;  $40.96 \pm 6.31$  vs.  $31.99 \pm 5.25$ , P = 0.00, respectively). Yoon and Son<sup>[31]</sup> used a Biorescue device (RM INGENIERIE, France) in their research to explore the effect of VR-based rehabilitation on balance control.<sup>[17]</sup> They found that VR-based rehabilitation significantly increased static balance and dynamic balance in patients who had undergone TKA.<sup>[31]</sup> Fung *et al*<sup>[17]</sup> used the activity-specific balance confidence scale to assess balance confidence in exercise. They found that VR-based rehabilitation could not offer significantly superior balance

confidence compared to conventional lower extremity exercise at 2 weeks.

### ROM

Five studies evaluated changes in knee ROM.<sup>[17,18,20,21,28]</sup> Fung *et al*<sup>[17]</sup> reported the change in active knee flexion and extension. However, they only report the percentage change from baseline to 2 weeks without any measures of variability, such as standard deviations. No significant

	Expe	rimen	tal	C	ontrol			Std. Mean Difference		Std. M	lean Difference	1	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV. Random. 95% CI	Year	IV. R	andom. 95% Cl	<u>î</u>	
3.1.1 within 1 m							2						
Piqueras 2013	-3.36	5.38	72	5.22	6.25	70	25.6%	-1.47 [-1.84, -1.09]	2013				
Yoon 2020	18.99	5.73	15	21.36	5.77	15	23.2%	-0.40 [-1.12, 0.32]	2020				
Subtotal (95% CI)			87			85	48.9%	-0.98 [-2.02, 0.06]					
Heterogeneity: Tau <sup>2</sup> =	0.48; Ch	i <sup>2</sup> = 6.	57, df =	1(P = 0)	0.01); 1	<sup>2</sup> = 85%	0						
Test for overall effect:	Z = 1.85	(P = 0	.06)	•									
3.1.2 3 m													
Piqueras 2013	-7	6.31	68	-10.86	8.72	65	25.8%	0.51 [0.16, 0.85]	2013				
Eichler 2019	7.5	1.2	48	7.5	1.6	39	25.4%	0.00 [-0.42, 0.42]	2019		-		
Subtotal (95% CI)			116			104	51.1%	0.27 [-0.23, 0.76]			-		
Heterogeneity: Tau <sup>2</sup> =	0.09; Ch	i² = 3.3	30, df =	1 (P = (	0.07); 1	<sup>2</sup> = 70%	6						
Test for overall effect:	Z = 1.06	(P = 0	.29)										
Total (95% CI)			203			189	100.0%	-0.34 [-1.31, 0.63]					
Heterogeneity: Tau <sup>2</sup> =	0.92; Ch	i <sup>2</sup> = 60	.67, df	= 3 (P <	0.000	01); l <sup>2</sup> =	= 95%			+ +	<u> </u>	+	-
Test for overall effect:	Z = 0.68	(P = 0	.49)	•		100				-4 -2		2	4
Test for subaroup diffe				f = 1 (P)	= 0.03	). $ ^2 = 7$	7.9%			Favours [experimen	ntal] Favours [c	[lonno:	

Figure 5: Forest plots of the meta-analysis of the effect of VR-based rehabilitation vs. conventional rehabilitation on TUG scores. CI: Confidence interval; TUG: Timed up and go; VR: Virtual reality; SD: Standard deviation; m: month.

change in knee ROM was found in their study. Gianola et  $al^{[20]}$  did not find a significant difference in knee ROM between baseline and 10 days. Jin *et al*<sup>[28]</sup> determined that knee ROM was significantly improved at 3 days, 7 days, and 14 days. In the study of Piqueras *et al*<sup>[18]</sup>, there was no significant difference in active knee flexion angle change between baseline and 10 days nor 3 months among the groups. However, VR-based rehabilitation offered significantly inferior active knee extension changes between baseline and 10 days compared to standard rehabilitation  $(0.2 \pm 2.8 \text{ vs. } 0.9 \pm 3.7, P = 0.045)$ . There was no significant difference in active knee extension between baseline and 3 months among the groups.<sup>[18]</sup> Bettger *et al*<sup>[21]</sup> found no significant difference in knee extension and flexion at 6 weeks between the two groups. Because the above five studies recorded ROM outcomes with different measurement methods and units, it is impossible to propose a pooled meta-analysis.

# Health-related quality of life

Two studies evaluated changes in health-related quality of life.<sup>[20,30]</sup> Eichler *et al*<sup>[30]</sup> found no significant difference between the two groups at 3 months, as measured by the SF-36 physical component scale and mental component scale. Gianola *et al*<sup>[20]</sup> discovered that early VR-based rehabilitation could not improve EQ-5D scores compared to the control 10 days after the trial.

## Discussion

The main purpose of this systematic review and metaanalysis was to evaluate whether VR-based rehabilitation improved the outcomes of patients after TKA. To the best of our knowledge, this is the first systematic review and meta-analysis to analyze the effect of VR-based rehabilitation on patients following TKA compared to conventional rehabilitation. For the first time, we found that VR-based rehabilitation improved pain, as measured by the VAS (low-quality evidence), and function, as measured by the WOMAC and HSS (high-quality evidence), but not postural control, as measured by the TUG (low-quality evidence).

Continuous moderate to severe post-operative pain is common following TKA, which impairs recovery outcomes.<sup>[34]</sup> The VAS is a common measurement tool for pain intensity and comprises a straight horizontal line of 100 mm length.<sup>[35]</sup> Patients were asked to report pain intensity from the left (no pain) to the right (worst imaginable pain).<sup>[36]</sup> A previous study has demonstrated an improvement in pain following TKA with active physiotherapy.<sup>[37]</sup> VR has been widely used to manage pain in a variety of settings.<sup>[38]</sup> Blasco *et al*<sup>[19]</sup> systematically reviewed relevant studies up to January 2018 and found that only two RCTs reported the effect of VR-based rehabilitation on pain after TKA.<sup>[17,18]</sup> They concluded that rehabilitation plans with VR devices failed to achieve superior outcomes in pain relief compared to rehabilitation without VR devices.<sup>[19]</sup> After including more RCTs that have been published recently in our meta-analysis, we proved for the first time that VR-based rehabilitation improved pain following TKA compared to conventional rehabilitation within 1 month, but not 2 to 3 months. However, significant heterogeneities were observed in all the comparisons of pain. Koo *et al*<sup>[39]</sup> found that long-term VR-based rehabilitation improved post-operative pain more than short-term VR-based rehabilitation.

Providing patients with a medium- and long-term quality of life, pain relief, and functional improvement is crucial for TKA postoperative management.<sup>[40]</sup> Post-operative rehabilitation following TKA promotes recovery and quality of life.<sup>[41]</sup> The early systematic review only included two published RCTs and concluded that VR did not improve self-reported functional performance with limited evidence.<sup>[19]</sup> In Martínez and Zavala,<sup>[42]</sup> all patients who received physical therapy training with VR for 6 weeks had decreased WOMAC scores. However, they did not adopt a control group. We included four articles that reported the WOMAC and two articles that reported the HSS in the meta-analysis. We confirmed that VR-based rehabilitation improved functional outcomes, including the WOMAC and HSS, compared to conventional rehabilitation.

The TUG was used to screen for fall risk in older patients using the guidelines of the American Geriatric Society and the British Geriatric Society.<sup>[43]</sup> Patients needed to stand up from a standard chair using their arms, walk three meters away, and then return and sit down on the chair again. A faster test time indicates better balance and functional results.<sup>[44]</sup> A meta-analysis involving 1021 patients reported that progressive resistance training could not improve TUG scores following joint arthroplasty.<sup>[45]</sup> Two RCTs reported TUG results in our study.<sup>[18,31]</sup> We found that VR-based rehabilitation provides no additional benefits in terms of TUG compared to conventional rehabilitation. However, only three RCTs reported TUG results, and high heterogeneity existed. It is necessary to conduct more RCTs with a high level of evidence.

The BBS is a common balance assessment tool that includes 14 items.<sup>[46,47]</sup> Each item consists of a five-point ordinal scale ranging from 0 to 4. Berg *et al*<sup>[46]</sup> confirmed that a score of 56 points indicates functional balance, whereas a score of <45 indicates a greater risk of falling. Only one article in our meta-analysis reported results of the BBS. Li *et al*<sup>[29]</sup> found that VR-based rehabilitation improved BBS scores compared to conventional CPM rehabilitation. Yoon and Son<sup>[31]</sup> confirmed that VR-based rehabilitation promotes balance control for patients following TKA by other method. The results from Fung *et al*<sup>[17]</sup> did not support this viewpoint. It is difficult to evaluate the pooled effect of VR-based rehabilitation on balance due to a limited number of high-quality RCTs. In addition, it is necessary to unify the evaluation methods.

Appropriate ROM is crucial for an ideal result following TKA. Physical exercise improves ROM after TKA.<sup>[48]</sup> Su<sup>[49]</sup> randomly assigned 27 patients following TKA into two groups: the experimental and control groups. Patients in the experimental group received rehabilitation activities and a Kinect-based virtual rehabilitation, whereas patients in the control group received conventional rehabilitation activities. After completing 6 days of rehabilitation, patients in the experimental group showed an improved average bending angle compared with the control group. Our review recorded ROMs with different measurement methods and units, so conducting a meta-analysis was impossible. Four articles in our study reported that knee ROM in the VR-based rehabilitation group was not superior to that in the conventional rehabilitation group.

Compared with a similar review reported by Blasco  $et al^{[19]}$ , our study has some original findings and strengths. First, with limited included studies and heterogeneous interventional designs, Blasco et al could not conduct a meta-analysis. However, after including more important RCTs published recently, we pooled analyzed the effect of VR-based rehabilitation on TKA patients with a meta-analysis. Second, they concluded that rehabilitation with VR has no advantage over conventional rehabilitation in terms of enhancing function, improving pain, nor increasing satisfaction following TKA. However, our study found that VR-based rehabilitation improved pain and function but not postural or balance control. This was the first systematic review and meta-analysis that reported the effect of VR-based rehabilitation on TKA.

Our study was not without limitations. First, the study protocols differed, including the intervention and control designs, the duration and frequency of rehabilitation, and the definition of VR-based rehabilitation. This may also contributed to the heterogeneity in our study. Second, although all the studies were RCTs, it was difficult to blind patients and therapists during rehabilitation, which may inevitably bias the self-reported outcomes. Third, owing to the limited sample size, the advantage of VR-based rehabilitation in TKA still needs more high-quality RCTs to be conducted.

## Conclusions

VR-based rehabilitation improved pain and function but not postural control following TKA compared to conventional rehabilitation. More high-quality RCTs are needed to prove the advantage of VR-based rehabilitation. As the COVID-19 pandemic continues, it is necessary to promote this rehabilitation model.

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#### **Conflicts of interest**

None.

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