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Efficacy of virtual reality-based interventions for patients with breast cancer symptom and rehabilitation management: a systematic review and meta-analysis

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ABSTRACT

Objectives To determine the effectiveness of virtual reality (VR)-based intervention on the symptoms and rehabilitation management in patients with breast cancer.

Design Systematic review and meta-analysis.

Study selection We included all eligible randomised controlled trials and quasi-experimental studies (published in English and Chinese).

Participants Patients with breast cancer (≥18 years) undergoing cancer treatment.

Interventions Any intervention administered to improve the symptoms and rehabilitation of patients with breast cancer. The control group was given conventional care.

Outcomes All outcomes were as follows: pain, fatigue, anxiety, depressive symptoms, cognitive function, and range of motion of upper limb in patients with breast cancer.

Data sources We searched PubMed, Embase, CENTRAL and SinoMed, four electronic databases, covering the database establishment period to January 2022.

Review methods Two reviewers independently extracted content and data consistent with the prespecified framework and assessed risk bias. Random-effects meta-analysis was used to pool data across trials. Meta-analysis was performed using Review Manager V.5.4.

Results A total of eight studies met the eligibility criteria and were included in this study. The combined effect size showed that VR was positive for improving patients' anxiety(standard mean differenc (SMD)=−2.07, 95% CI= (−3.81 to −0.34), I^2=95%) and abduction of upper limbs (MD=15.54, 95% CI= (12.79 to 18.29), I^2=0%), but fatigue (SMD=−0.92, 95% CI= (−4.47 to 2.62), I^2=99%) was not. Qualitative analysis showed VR improved patients' depressive symptoms, pain and cognitive function.

Conclusions VR technology has a good effect on symptoms and rehabilitation management of patients with breast cancer, but the quality of evidence is low, and the sample size is small. To date, there are few intervention studies, therefore, giving precise recommendation or conclusion is difficult. We have a favourable view of this, and more clinical studies are

Strengths and limitations of this study

► Unlike previous systematic reviews that focused on many types of patients with cancer, this is the first review that aims at investigating the effectiveness of virtual reality in patients with breast cancer to evaluate the relative safety and effectiveness of this new technology.

► Due to the diversity of research design, we used the random effect model for analysis.

► Faced with the COVID-19 pandemic period, the intervention based on virtual reality provides patients to undergo rehabilitation effectively at home and reduce the risk of infection.

► High heterogeneity in some outcome measures due to different measurement tools, low quality of included studies and small sample size limit the further promotion of the results, resulting in a risk of bias.

► The quality of the included literature is low, the long-term effect on patients is still unclear, there is a lack of literature support with a higher level of evidence.

needed in the future to improve the credibility of the results.

INTRODUCTION

Breast cancer is the most commonly occurring cancer in women.[1] There were over 2 million new cases and nearly 630 thousand deaths globally in 2018.[2] Moreover, according to the prediction, new patients with breast cancer will increase by more than 46% by 2040.[3] In recent years, there has been a remarkable improvement in breast cancer-related survival rate and life quality,[4] because of the accessibility to various treatment options and rehabilitation options, for instance, early breast cancer screening, chemotherapy radiotherapy, surgical therapy and comprehensive treatment rehabilitation

management.[5–9] However, the long-term breast cancer disease progression and the treatment have some adverse effects, which can cause some physical and psychological negative consequences.[10] These possible long-term adverse effects include somatic symptoms such as limited joint range of motion, pain and psychological distress such as fatigue, anxiety and depressive symptoms.[11–13] Simultaneously, these symptoms and negative emotions may further cause cognitive dysfunctions for the patient, leading to poor predictive outcomes and affecting all aspects of their life.[14 15]

Some adjuvant treatments are used for rehabilitation management of patients with breast cancer to improve symptoms, side effects and the quality of life.[16] This process is often carried out through traditional physical therapy and occupational therapy to improve the patients' symptoms and perform rehabilitation management.[17] However, these traditional methods are time-consuming, cumbersome, and cost a lot, and the results often depend on the medical staff's actual capabilities.[18] Moreover, traditional rehabilitation therapy is primarily mechanical repetitive training, which lacks interest and motivation.[19] Patients often lose interest in this process, which affects the training effect of patients. So the limitations of traditional rehabilitation training prompted the emergence of new and effective methods.

With the rapid development of computer science, more and more modern technologies are applied to managing symptoms and rehabilitation of patients with breast cancer, and it is continuously developing.[20]

Virtual reality (VR) is mainly used as a brand new rehabilitation therapy for patients with breast cancer. The concept of VR was first proposed in the 1960s and gradually rose at the end of the 20th century, and it is an artificial intelligence technology based on multidisciplinary cooperation.[21]

It uses the computer as the core architecture, calculates and simulates a three-dimensional (3D) virtual environment, and combines with other somatosensory devices (such as somatosensory handle, sensing helmet, 3D glasses) to make up the gap between the virtual environment and reality.[22]

It allows interactive feedback between the user and the virtual environment, providing the user with visual, auditory, tactile, and other signal stimuli to produce their feelings. The features of VR are summarised into '3i'. They are immersive, interactive and imaginative.[23] Compared with the traditional 'viewing from the outside—in silico operation', 'VR emphasises human beings' dominant role in virtual environments. With the high-speed development of VR technology, its connotation is also further broadened. Based on VR, the concepts of augmented reality, mixed reality were extended.[24] Although VR technology is more diversified, it is mainly applied to patients with breast cancer in immersive experiences using headgear and computer games.

In recent years, VR has received increasing attention as a symptom and rehabilitation training approach to address pain reduction, fatigue, anxiety, depression and cognitive dysfunction in different groups. It has been applied for physical rehabilitation management of some diseases, such as stroke, Parkinson's, rectal cancer and prostatic cancer.[25–28] Moreover, it has indeed received good results, and the quality of life of these patients has been dramatically improved. Considering that patients with breast cancer have similar physical and mental burdens, it is feasible to attempt VR into them. As for patients with breast cancer, VR technology was gradually introduced into American scholars' clinical intervention research in the early 21st century.[28] However, there are few intervention studies for patients with breast cancer. Many of them are still in clinical trials, and there is no systematic review to summarise and analyse them. There is no specific intervention strategy. Existing systematic reviews primarily focused on the inclusion and analysis of mixed samples of patients with cancer.[29]

Therefore, we need to focus on specific populations of patients to be selected in research. Thus, doubts could be raised as to whether VR treatment methods for breast cancer can improve these symptoms; and whether the rehabilitation of patients is effective is worth studying. For this reason, we aimed to perform a meta-analysis as a scientific method to investigate the effects of this uncertain treatment using statistical methods to examine whether VR training is practical for patients with breast cancer symptoms and rehabilitation management. According to the current guidelines for patients with breast cancer, we mainly focus on those who receive breast surgery or receive radiotherapy or chemotherapy on Tumor Node Metastasis classification (TNM) 1–4 stage.[30] Based on the data analysis findings, we can make an objective evaluation and analysis of VR technology in the rehabilitation and symptom management of patients with breast cancer, hoping to provide a reference for the Application of patients and the clinical decision making of medical staff.

METHODS
Search strategy
We checked up to three English databases (PubMed, Embase and CENTRAL), and one Chinese database (SinoMed) from the establishment of databases to November 2020, with the following Mesh terms and text words: ("Breast Neoplasms" OR "Breast Cancer Lymphedema" OR "breast tumor*" OR "breast cancer") AND ("Virtual Reality" OR "Virtual Reality Exposure Therapy" OR "simulation environment"). Online supplemental appendix 1 shows the exact searching strategy. Finally, based on the above results, we performed a snowballing approach to search, screen, and examine papers, classifying them as potentially eligible studies.

Eligibility criteria
Types of studies
We included all eligible randomised controlled trials (RCTs), and quasi-experimental studies (published

in English and Chinese), at least one of which was an ongoing VR training programme for inclusion in the review.

Types of participants

Our inclusion population was required to meet the following criteria: (1) breast cancer diagnosed by pathological analysis (TNM stage I–IV); (2) age ≥18 years old; (3) after surgery ongoing chemotherapy or radiotherapy. We also developed exclusion criteria for the participants: (1) brain primary (patients may have adverse reactions to VR); (2) combined with other severe diseases (such as severe heart disease, hypertension); (3) previous psychiatric illness or cognitive impairment; (4) primary limb movement disorders; (5) visual and auditory impairment.

Types of interventions

The trial group participated in the organised and systematic intervention project based on VR technology for patients with breast cancer. The primary intervention goal was to reduce the psychological disorder, dysfunction, and pain of patients.

The intervention experiment based on VR needs to meet the following core conditions:

1. Using computer-generated human-computer interactive intervention means in the virtual environment, such as VR glasses and headwear equipment.
2. Patients immerse themselves in the virtual environment constructed by electronic equipment.
3. Patients can perceive, feel and interact in a manner that is similar to a physical place.
4. They can achieve effects by combining stimulation over multiple sensory channels such as vision, sound, touch and perception to produce a corresponding stimulus.

And the potential comparison groups included any format of rehabilitation intervention, like exercise and usual care.

Types of outcomes

Due to the different focus of the original research, the leading evaluation indicators may be various. To show the improvement of outcomes for patients by VR as comprehensively as possible and provide a reference for subsequent studies, we selected as many outcomes as possible under objective and fair evaluation conditions. The outcomes included: the patient's anxiety, fatigue, depressive symptoms, pain, cognitive function and abduction of upper limbs. The measurement tools for outcomes are shown in the characteristics of the included studies.

Data collection and analysis

Selection of studies

Two review authors independently screened all search results (title, abstract) in the database to identify studies that could be included in this paper. After initial screening, the review authors performed a full-text evaluation to determine the literature for inclusion. When disagreements occurred, they discussed the disparities and resolved them. If consensus was not reached after discussion between the two, it was decided by the third author independent arbitration. If necessary, we contacted study authors for specific information.

Data extraction and management

Two review authors independently extracted data onto a predesigned data collection form, including the trial setting, inclusion and exclusion criteria, study population, interventions, outcome measures and final results of the papers. Both review authors, before data extraction, were given detailed instructions and participated in training sessions. Any disagreements or discrepancies regarding data extraction were resolved through discussion, and a third reviewer was consulted in case of any disagreement.

Assessment of risk of bias in included studies

We performed the risk of bias (ROB) of RCTs using Cochrane Collaboration ROB-2.[31] The overall assessment was recorded as high, low, and some concerns. Synthesis of ROB plots was done using online software Robvis (visualisation tool).[31] We used Joanna Briggs Institute (JBI) critical appraisal checklist for quasi-experimental studies evaluated and included the before-and-after study.[32]

Data analysis

All analyses were performed using RevMan V.5.4 (Cochrane Collaboration, http://ims.cochrane.org/revman). Heterogeneity was assessed using Cochran's Q test and quantified with the I^2 test. A random-effects model was applied to calculate the pooled results if $I^2 \geq 50\%$; otherwise, a fixed-effects model was used. Forest plot graphics were generated to present the pooled effect. The mean difference (MD) and standard MD (SMD) with corresponding 95% CI were used to calculate the effect size. SMD was calculated where the same outcome was reported but using different measurement tools. All tests are two-sided, and $p<0.05$ was considered to be statistically significant.

Dealing with missing data

There were no missing data for any of the included articles.

RESULTS
Search process

After searching in four databases, we retrieved 3058 articles. For these documents, we conducted a duplicate check, preliminary screening, and full-text reading for screening. Finally, eight papers met the criteria of this meta-analysis. Six were RCTs, and two were before-and-after studies. Figure 1 shows the detailed search process and results.

Critical appraisal of quality

Figure 2 shows the quality assessment of the included studies: 3 RCTs[33–35] judged by ROB-2 have a high ROB, 1[36] have a low ROB, while the remaining 2[37 38] studies showed the uncertain risk bias. The following were the primary
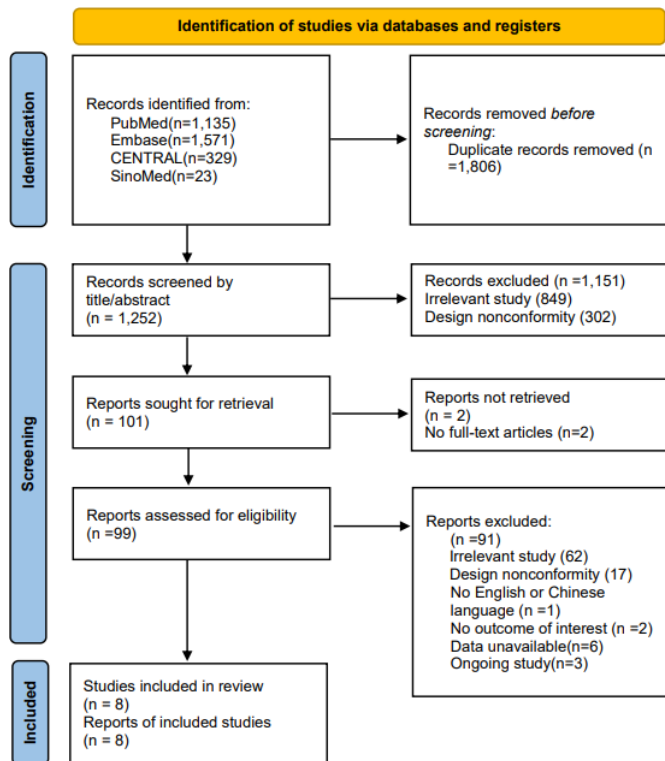
Figure 1 Flow chart for study selection according to PRISMA Declaration 2020. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

sources of bias: deviations from intended intervention, differences in outcome measurement and unclear randomisation process. In summary, the quality of the included RCTs was considered as having a high ROB. 2[39 40] before-and-after studies judged by the JBI tool show the central bias exists in: comparison receiving similar care and multiple measurements of the outcome (table 1).

Study characteristics

The essential characteristics of the included studies are shown in table 2. The quality of the eight studies met our inclusion criteria. Three studies were from China,[34 35 40] and the others were from the United States,[39] Jordan,[37] Italy,[33] Turkey[36] and Australia.[38] Two of them were before-and-after controlled trials, and the other six were RCTs. The research was conducted in specialised wards and

Figure 2 Quality assessment of the included studies.

cancer centres of hospitals. The number of participants ranged from 6 to 120. All participants were patients with breast cancer who met the inclusion criteria. VR intervention included both immersive and non-immersive formats, and the duration of the intervention ranged from 20 min to 3 months. The studies assessed VR-based interventions' impact on health-related outcomes, including anxiety, depressive symptoms, fatigue, pain, cognitive function and abduction of upper limbs.

Outcome analysis

Due to the limitation of research type and significant heterogeneity between groups, we only selected anxiety, fatigue, and abduction for meta-analysis. As for the remaining outcomes, we chose the form of qualitative analysis. We detailed the research form, time, equipment, and content of each study in table 2. Although we could not conduct a meta-analysis, we also analysed and expounded on their strengths and limitations.

Anxiety meta-analysis

Three studies[33 37 38] evaluated the impact of VR on anxiety of patients with breast cancer. Compared with the control group, the results showed that VR-based intervention had a significant effect (SMD=−2.07, 95% CI= (−3.81 to −0.34), p=0.02, figure 3). Heterogeneity was considerably high (I^2=95%).

Abduction meta-analysis

Two studies[35 36] evaluated the impact of VR on abduction of patients with breast cancer. Compared with the control group, the results showed that VR-based intervention had a significant effect (MD=15.54, 95% CI= (12.79 to 18.29), p<0.00001, figure 4). Heterogeneity was considerably low (I^2=0%).

Fatigue meta-analysis

Two studies[33 34] evaluated the impact of VR on fatigue of patients with breast cancer. Compared with the control group, the results showed that VR-based intervention had no significant effect (SMD=−0.92, 95% CI= (−4.47 to 2.62), p=0.61, figure 5). Heterogeneity was considerably high (I^2=99%).

Depressive symptoms analysis

In two studies, participants were distracted by training in a recovery game in a virtual environment, and both before-and-after study[39] and RCT[33] showed improvement in depressive symptoms. At the end of the intervention, the depression symptoms scores (MD) of patients in the before-and-after study decreased by 8.3 compared with baseline data (p<0.05), and there were differences between the VR and control groups after the intervention in the RCT (p<0.05). The results were statistically significant.

Pain analysis

Three studies focused on patients' pain symptoms after the VR intervention, one before-and-after study,[39] and

Table 1 Results of critical appraisal for quasi-experimental studies

Questions (potential bias and threat)	House et al[39]	Chen et al[40]
1. Is it clear in the study what is the 'cause' and what is the 'effect'?	Yes	Yes
2. Were the participants included in any comparisons similar?	Yes	Yes
3. Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?	No	Unclear
4. Was there a control group?	Yes	Yes
5. Were there multiple measurements of the outcome both pre and post the intervention/exposure?	Yes	No
6. Was follow-up complete and if not, were differences between groups in terms of their follow-up adequately described and analysed?	Yes	Yes
7. Were the outcomes of participants included in any comparisons measured in the same way?	Yes	Yes
8. Were outcomes measured in a reliable way?	Yes	Yes
9. Was appropriate statistical analysis used?	Yes	Yes

two RCTs[36 37] showed a reduction in patients' pain scores. At the end of the intervention, patients' pain scores (MD) in the before-and-after study decreased by 1.5 compared with baseline ($p<0.05$). There were differences in pain after intervention between the VR and control groups in two RCTs ($p<0.05$). The results were statistically significant.

Cognitive function analysis

Two before-and-after studies[39 40] examined the effects of VR on patients' cognitive function, showing significant improvements in executive function, language function, memory and visual function. The results were statistically significant.

DISCUSSION

This systematic review and meta-analysis evaluated the application effect of intervention based-on VR in patients wih breast cancer. Consistent with previous research,[41] the results showed that compared with traditional breast cancer care, patients' anxiety, depressive symptoms, pain, cognitive function and abduction of the upper limbs were improved with a statistical significance. However, the pooled effect showed that VR-based intervention had no effect on fatigue.

Our results showed that VR had a significant effect on anxiety among patients with breast cancer. With the transformation from the traditional medical system to a biopsychosocial medical network, much more attention has been paid to the role of anxiety in the aetiology and prognosis of breast cancer.[42] The prevalence of anxiety among patients with breast cancer was 41.9%.[43] The previous study assessed the effectiveness of VR for patients with cancer, and their results showed VR had no significant effect on reducing anxiety in patients.[29] The difference

in results might be that we focused on patients with breast cancer, who were more uniform and had minor variations. Our results indicated that the heterogeneity of the included studies was significant. Due to the limited number of articles, we were unable to conduct sensitivity analysis to find the source of heterogeneity. According to the study design, we found that heterogeneity might exist in the specific treatment types of patients undergoing VR intervention, different pathological stages of cancer, small sample size, inconsistent equipment used and different or unclear frequency and duration of intervention. Like anxiety, patients with breast cancer usually get mental problems and physical symptoms. A total of 97% of patients with breast cancer report experiencing depression symptoms and pain. Our review also included the effect of VR on depressive symptoms. In both studies analysed, the VR treatment had a reducing effect on depressive symptoms. Because of the different types of research and lack of data, we could not show their combined effect sizes. We believe the possible mechanism behind VR's effect on the above symptoms is the distraction mechanism. According to Buhle et al,[44] the mechanism of distraction is different from placebo. Their MRI analysis showed distraction effectively suppressed pain processing in the brain, while placebo had no significant effect on pain processing. We hypothesise VR reduces pain through distraction, thereby improving patients' psychiatric symptoms during treatment. As mentioned before, our study was limited in many aspects, such as the type of study and sample, so we should treat this result with caution.

Our results showed that VR had a significant effect on the abduction of upper limbs among patients with breast cancer. Bleeding, effusion, necrosis of skin flap and upper limb oedema often occur after radical breast

Table 2 Characteristics of the included studies

Study (country/year)	Design	Target population	Disease stage/ age	Frequency (days/week)	Duration/ session (min)	Intervention time (weeks)	VR method	Study outcome	Study results
House et al (USA/2016)[39]	Before-and-after study	Postsurgical breast cancer women (n=6) with pain in the upper arm.	Unknown Age:57.8±20.4	2	20–50	8	The BrightArm Duo Rehabilitation System consists of a low-friction robotic rehabilitation table. A computerised forearm supports a display, a laptop computer for the therapist station, a remote clinical server, and a library of custom integrative rehabilitation games. It tracks arm position and grasping strength while patients play three-dimensional (3D) custom integrative rehabilitation games. Training difficulty increased progressively in game complexity, table tilt, and session length.	BDI-II-depression symptom-decreased; BVMT-R/HVLT-R/TMT/NAB- cognitive function-improved; NRS-pain-decreased; Mechanical Goniometers-ROM-improved	PS PS PS PS
Chen et al (China/2019)[40]	Before-and-after study	Breast cancer women (n=80) after surgery were hospitalised for chemotherapy.	II–III Age range:40–60	5	20–30	8	Patients with its motion-sensing controller and computer to build virtual cognitive rehabilitation training system, memory, executive ability, the training of the information processing speed and concentration of four modules, with the help of virtual scene and the virtual objects, through a variety of tasks such as puzzles, tai chi, a virtual maze game, improve patients' cognitive function, and real-time information feedback and rehabilitation information support.	MoCA -cognitive function-improved	PS

Table 2 Continued

Study (country/year)	Design	Target population	Disease stage/age	Frequency (days/week)	Duration/session (min)	Intervention time (weeks)	VR method	Study outcome	Study results
Bani Mohammad et al (Jordan/2018)[37]	RCT	Female patients with breast cancer (n=80) at a specialised cancer centre	II-III Age:51.99±10.34	When giving morphine	15	When giving morphine	The CG (n=40) did not receive VR treatment. The VG (n=40) chose from two scenarios on a CD-ROM, which included deep-sea diving 'Ocean Rift' or sitting on the beach with the 'Happy Place' track. Then, the patients wore a head-mounted display with headphones. The PI remained near the participants during the VR session. The VR exposure session was ended at the peak time of painkiller efficacy.	VAS-pain-decreased; SAI-anxiety-decreased.	BS BS
Chirico et al (Italy/2019)[33]	RCT	Female patients with breast cancer (n=94) were receiving chemotherapy.	I-III Age: VG:55.18±5.7 MTG:55.7±5.26 CG:56.2±6.79	During each chemotherapy	20	During each chemotherapy	The CG (n=34) received routine care, and the MTG (n=30) received music therapy based on CG. The VG (n=30): The VR equipment consisted of a headset and an ahead movement tracking system. Participants explore the island through the relaxing landscape created on the Second Life platform through forests, animal observation, mountain climbing, and swimming.	SAI-anxiety-decreased; SV-POMS(T/D/F)-depression symptom/fatigue-decreased	BS BS
Feyzioğlu et al (Turkey/2020)[36]	RCT	Breast cancer women (n=36) had undergone surgery.	Unknown; Age: VG:50.84±8.53; CG:51.00±7.06	2	45	6	The VG (n=19) received tissue massage, passive mobilisation, and Xbox360Kinect video game treatment. The patient performed activities based on VR boxing, darts, and other games; the CG (n=17) received standard upper limb physical therapy treatment, including scar tissue massage and passive mobilisation.	VAS-pain-decreased; Digital Goniometer-ROM-improved.	PS PS

Continued

Table 2 Continued

Study (country/year)	Design	Target population	Disease stage/age	Frequency (days/week)	Duration/session (min)	Intervention time (weeks)	VR method	Study outcome	Study results
Jimenez et al (Australia/2018)[38]	RCT	Female patients with breast cancer (n=37) received radiotherapy.	Unknown; Age range VG:35–74 CG: 35–74	Unknown	60	18	The VG (n=19) used the VERT system (Version 2.9) to provide basic technology, anatomical knowledge, and radiation dose information about RT for patients. The CG (n=18) received regular health education on radiotherapy knowledge.	STAI-S-anxiety-decreased.	PS
Jin a et al (China/2018)[35]	RCT	Female patients with breast cancer (n=120) undergoing surgery.	I–III Age range 20–50	6	30	12	The VG (n=60) used a professional rehabilitation platform; through the virtual and VR somatosensory equipment (helmet, joystick, data gloves), patients can choose their rehabilitation games for training. The CG (n=60) received traditional rehabilitation training.	SF-36-pain/fatigue-improved	BS
Jin b et al (China/2018)[34]	RCT	Female patients with breast cancer (n=76) received surgery.	II–III; Age range 33–69	14	15–30	12	The VG (n=38) selected appropriate training methods for rehabilitation according to the patients' muscle strength characteristics in different postoperative rehabilitation periods. The system includes sensors (HTC), upper limb rehabilitation devices, and a game platform (Unity 3D). The CG (n=38) received routine rehabilitation training under the guidance of nurses.	Mechanical Goniometers-ROM-improved	BS

BS: The comparison between the two groups was statistically significant.
PS: Outcome improved postintervention, but intergroup results were not statistically significant, or there was no control group.
BDI-II, Beck Depression Inventory; BVMT-R, Brief Visuospatial Memory Tes; CG, control group; HTC, Heat Transfer Compound; HVLT-R, Hopkins Verbal Learning Test; MoCA, Montreal Cognitive Assessment; MTG, music therapy group; NAB, neuropsychological assessment batter; NRS, Numeric Pain Rating Scale; RCT, randomised controlled trial; ROM, range of motion; SAI, state anxiety inventory; SF-36, 36-Item Short Form Survey; STAI-S, State-Trait Anxiety Inventory-State; SV-POMS(T/D/F), Short Version of Profile of Mood States in tense, depressive, and fatigue; TMT, trail making test; VAS, Visual Analog Scale; VG, virtual group; VR, virtual reality.
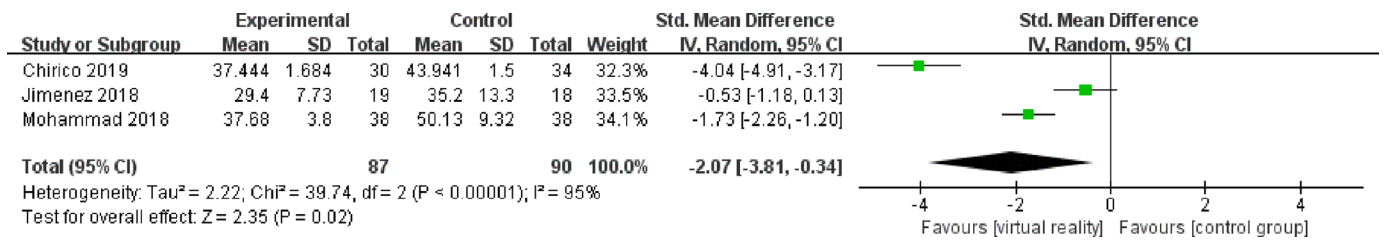
Figure 3 Effect of VR-based interventions on anxiety. IV, inverse variance; VR, virtual reality.

cancer surgery, which will cause upper limb dysfunction such as limited shoulder joint activity and limb weakness, and significantly reduce the quality of life of patients.[45] VR as a rehabilitation tool has been very mature. Application in improving the range of motion of patients' upper limbs, especially in stroke patients, has been well verified.[46] Our results suggested that VR as a rehabilitation tool could improve some aspects of patients' upper limb movement. Still, we need more extensive sample size trials to confirm its long-term effects. VR may not be the only influential factor; it may need other auxiliary tools to best use its effects.

Cancer-related fatigue has been documented as one of the most distressing symptoms reported by breast cancer survivors. It affects functioning and impacts quality of life. Possible causal factors include physical conditions, affective and cognitive states, proinflammatory cytokines and metabolic factors.[47] Our study found that VR had no effect on fatigue among patients with breast cancer, which was contradictory to the findings of Zeng et al,[29] who reported that VR-based intervention was related to a statistically significant decline in fatigue scores among patients with breast cancer. The possible reason for the discrepancy may be related to the differences in participants' characteristics. In addition, this may be related to the small sample size of literature included in the study, resulting in a significant bias. More strategies need to be explored to help patients with breast cancer simultaneously manage the level of fatigue.

A total of 16%–75% of patients with breast cancer receiving chemotherapy have some degree of cognitive impairment.[48] Cognitive impairment seriously affects patients' quality of life, even more than the recurrence and metastasis of breast cancer itself. Two before-and-after studies examined the cognitive improvement of VR in patients with breast cancer with improved vision, memory, executive function and language function after the intervention. Due to technical reasons, we failed to conduct a combined effect size analysis, but from the data

analysis of the before-and-after study, VR is beneficial to the cognitive function of patients. The primary characteristic of VR is immersion, which enhances the subject's heart rate and activates brain circuit functions. In particular, it acts on the midline θ of the brain's forehead, including the frontal lobe and the left temporal area, bringing a pleasant emotional experience to subjects, activating the attention of related brain networks and improving motor integration and spatial orientation functions.[49]

To sum up, in this context VR uses immersive experience to intervene and achieve positive effects for patients with breast cancer. The devices which were used are: wearable helmets, 3D glasses, somatosensory operating devices, smart displays and computers. Subjects can interact cognitively or physically in a computer-generated virtual environment in real time to achieve their goals. An immersive tool changes patients' focus of attention, provides a positive and pleasant experience, and improves progress. Because of the interactivity of VR, patients enhance the effectiveness of an intervention in the real-time interaction of VR. This may be related to activating the midbrain marginal dopaminergic pathway and VR technology stimulation in the interaction between patients and VR.[50] The brain's reward mechanism can improve the attractiveness of participating in the intervention, enhance patients with breast cancer interest, and make patients more like this form. VR has the characteristics of real-time in virtual environment. Not only can real-time monitor the behaviour and physiological response of patients, background data operation and guardians observe the transmission of stimulation in the virtual environment and comprehensively control the duration and intensity of rehabilitation.[51] The above utility mechanism improves the positive experience, attention, interaction and participation of patients to a certain extent. It carries out rehabilitation in a real-time dynamic monitoring environment to improve patients' compliance, promote the rehabilitation of patients with breast cancer and improve their prognosis.
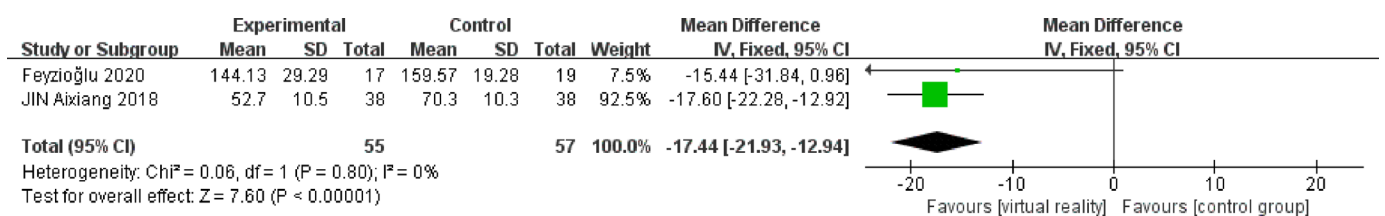

Figure 4 Effect of VR-based interventions on the abduction of upper limbs. IV, inverse variance; VR, virtual reality.
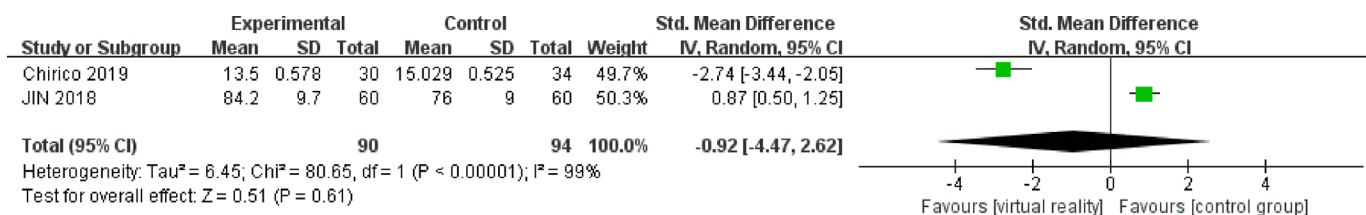
Figure 5 Effect of VR-based interventions on fatigue. IV, inverse variance; VR, virtual reality.

Direction for future research and practice

The discussion shows VR for breast cancer symptom management and rehabilitation intervention methods are worth learning and promoting. With the rapid development of 5G communication technology, artificial intelligence and Internet of Things technology, VR methods are bound to be more widely used and will receive technological innovation. Around the world, some countries have begun to formulate relevant laws and policies to give VR technical and economic support and policy inclination to accelerate industrial integration and put the new VR technology into clinical practice in medical and healthcare as soon as possible.[52]

According to our research results, we state the following directions for further research. The Use of VR Security Question. When using a VR device, subjects are immersed in a virtual environment and often ignore the potential dangers in the actual scene. There is a risk of accidental injury and falling. Therefore, they should be monitored during use. At the same time, professionals should evaluate and modify their environment to ensure patient safety. Simultaneously, the articles retrieved in our systematic review rarely involve safety evaluation indicators, so we did not use them as outcome indicators. In the follow-up research, the safety evaluation system of VR application in patients can be constructed and applied. Be alert to the potential adverse effects of VR. The highly immersive nature of VR stimulates sensory nerves, which may lead to adverse reactions such as blurred vision, dizziness, nausea and vomiting. Although the existing short-term intervention studies have not clearly defined it as an adverse event, long-term effect monitoring is still needed to avoid possible health problems and addiction caused by long-term use. The hardware and ecological construction are not yet mature. The application of VR to breast cancer is still in its infancy. Most VR products on the market are not specifically developed for patients with breast cancer. The clinical integration is low, ecological resource construction is not mature and patients' targeted demands cannot be met. It can be low selectivity. It is suggested that a multidisciplinary team should be formed to develop VR hardware and ecological communities for patients with breast cancer, build a more extensive resource library, enrich the functions of VR, and give patients more choices to maximise the benefits. During the COVID-19 pandemic, the social activities of the population were more alienated. This has demonstrated the importance of remote treatment systems when in-person patient-doctor contact is not possible. Because of the convenience and mobility of breast cancer intervention based on VR, patients can also be treated at home, reducing the risk of infection when going out and alleviating the feeling of social isolation. Telemedicine technology based on VR may become a trend to improve the utilisation efficiency of medical resources.

Limitations

This study has some limitations that need to be addressed, and which is why we need to interpret the results with caution. First of all, the types of studies included were relatively diverse, so we could not analyse the combined effect size in some outcomes. Although the qualitative analysis was carried out and the results were positive, we should treat it with caution because there was no quantitative analysis result. Second, we clarified and discussed the staging of patients with breast cancer. Most patients were in stage II–III, and the staging of patients in some of the included studies was unclear. The specific form of VR therapy that patients received also varies, so we cannot recommend its use for specific clinical populations, but based on our findings, we believe VR has significant benefits for patients with mental symptoms. VR interventions included in the study are different in terms of intervention time, frequency, and specific intervention form, so there is heterogeneity. The small sample size and number of participants in our study may lead to considerable differences between groups. And for this reason, we were unable to check for publication bias in this study. In the future, we suggest researchers conduct multi-centre RCTs to seek higher-quality evidence to prove the effect of VR on patients with breast cancer.

CONCLUSION

The systematic review showed that VR-based interventions improved anxiety, depressive symptoms, pain, cognitive function and abduction of upper limbs in patients with breast cancer, but not fatigue. Due to this paper's limitations and extensive sources, we were unable to carry out specific recommendations and conclusions. In the future, large-scale pilot studies on symptom management and rehabilitation in patients with breast cancer should be carried out to explore its applicability and feasibility in patients with breast cancer.

Patient consent for publication Not applicable.

Ethics approval This study does not involve human participants.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement All data relevant to the study are included in the article or uploaded as online supplemental information. All the data are avilable attached this paper.

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