Review Article

Meta-Analysis of the Efficacy of Virtual Reality–Based Interventions in Cancer-Related Symptom Management

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Abstract

Background. This meta-analysis summarizes the results from recent studies that examined the use of virtual reality (VR)–based interventions on health-related outcomes in patients with cancer, and quantitatively evaluates the efficacy of VR-based interventions. Findings of this meta-analysis can provide direction for future symptom management research. *Methods.* The search terms included a combination of "virtual reality" OR "virtual environment" OR "head-mounted display" with "oncology" OR "cancer." Three databases (Medline, PubMed, and CAJ Full-text Database), one search engine (Google Scholar), and the website of ResearchGate, covering the period from December 2013 to May 15, 2019, and including articles published in both English and Chinese, were searched. Data synthesis used the RevMan 5.3 to generate pooled estimates of effect size. *Results.* A total of 6 empirical studies met the eligibility criteria. VR-based interventions had statistically significant effects on reducing symptoms of anxiety, depression, pain, and cognitive function, whereas statistically significant benefit was observed for fatigue ($Z = 2.76$, $P = .006$). *Conclusion.* Most recent studies have primarily examined VR-based interventions for symptom management in the acute stages of cancer care. However, the management of late and long-term side effects is central to cancer survivorship care. There is burgeoning empirical support for further research to evaluate the efficacy of VR-based interventions in cancer rehabilitation.

Keywords

virtual reality, cancer care, meta-analysis

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Introduction

The incidence of cancer is increasing globally and the 5-year relative survival rate for individuals with cancer is 67%.[1] As more cancer patients live longer after treatment, long-term or late effects of cancer and its treatment are more commonly seen in cancer survivors.[2] The long-term side effects of cancer and cancer treatment may include a number of physical and psychological consequences, such as pain, fatigue, anxiety, depression, and cognitive dysfunction.[3-5] Psychological distress has been found to be negatively associated with cognitive function in cancer patients.[4-6] Research has also found that cancer-related fatigue and mood changes, such anxiety and depression, significantly affect cancer patients' cognitive functioning and lower their quality of life.[7,8]

Due to recent technology advancements, the development and application of modern technology in the health care field offers new and noninvasive approaches for cancer-related symptom management.[9] Virtual reality (VR) includes a computer capable of real-time animation, controlled by a set of sensory input devices, a position tracker, and a head-mounted device for visual output.[10] There is growing interest in the use of VR-based therapies in

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multidisciplinary symptom management to address pain reduction, cancer-related fatigue, anxiety, depression, and cognitive dysfunction.[11-13] While 2 recent reviews have synthesized VR exercises for anxiety and depression management or VR as a distractive intervention to relieve pain and distress during medical procedures,[14,15] neither of these recent reviews focused on the cancer population. A single older review was previously published that described the use of VR-based interventions in cancer care, but this review only included reports published prior to December 2013.[9]

Therefore, the aim of this meta-analysis was to report on the most recent studies using VR-based interventions for symptom management in patients with cancer, and to quantitatively evaluate the efficacy of VR-based intervention in cancer-related symptom management. Findings of this meta-analysis can provide direction for future research.

Methods

The search terms included a combination of "virtual reality" OR "virtual environment" OR "head-mounted display" with "oncology" OR "cancer." These search terms used in this meta-analysis were identified from previous studies' titles and abstracts. Three databases (Medline, PubMed, and CAJ Full-text Database), one search engine (Google Scholar), and the website of ResearchGate, covering the period from December 2013 to May 15, 2019, and including articles published in both English and Chinese, were searched. Inclusion criteria were patients who were diagnosed with adult-onset (aged 18 years or older) cancer. Interventions included were any type of VR-based interventions (immersive and nonimmersive virtual environment) for cancer patients. Types of studies included randomized controlled or case-controlled trials, and quasi-experimental studies. For each study, data were extracted from the original article by the first author (YZ), then independently verified by a co-investigator (JZ). Disagreements were resolved by a third author. Data synthesis used the Cochrane Collaboration Review Manager (RevMan 5.3; https://community.cochrane.org/help/tools-and-software/revman-5) to generate pooled estimates of effect size.

This meta-analysis used the 8-item quality scale to assess risk of bias of each included study. This tool was developed and used in previous studies[15,16]: these items including whether randomization procedure adequately described or not; with control group or not; outcomes measured before and after the intervention; retention-dropouts less than 30%; missing data analysis conducted; whether power analysis was conducted to determine the appropriate sample size; and with follow-up assessment or not. Each item was rated either as "positive" (low risk of bias) or "negative" (high risk of bias), the total score for each included study was summarized across all positive scores. A median score of 4.5 or above within each study was considered as "high quality and at low risk of bias."[15,16]

Results

Study Selection and Characteristics

Of the 293 studies identified through searching the 3 databases, 6 studies were eligible for the meta-analysis. Figure 1 shows the article search process and final study selection results.

The characteristics of the included studies are shown in Table 1. Of the 6 studies, 1 was a randomized controlled trial,[17] 1 was a case-controlled trial,[13] and the others were mainly a pre-post-test study design with a single arm.[11,12,18,19] In terms of study settings, only 2 studies were conducted at outpatient cancer care centers, while the others were conducted in hospital inpatient settings. The number of subjects ranged from 6 to 97. All participants were adult cancer patients/survivors. VR interventions included both immersive and nonimmersive formats and the duration of the interventions varied from 30 minutes to 16 weeks. All studies examined the effects of VR-based interventions on health-related outcomes, including anxiety, depression, fatigue, pain reduction, cognitive function, and physical fitness.

Quality and Risk of Bias Assessment

This meta-analysis used the 8-item quality and risk of bias assessment tool suggested by Zeng and colleagues.[15] Table 2 presents the results of the rating scores of each study. Only 1 study had a low risk of bias.[17] All of the other studies had a high risk of bias, most frequently due to the following: no randomization, no power analysis to calculate the appropriate sample size, missing information to discuss strategies to deal with missing data, and a lack of follow-up assessment (Table 2).

Overview of VR-Based Interventions to Relieve Cancer-Related Symptoms

Figure 2 shows that VR-based interventions had positive effects on reducing symptoms of anxiety (standardized mean difference of −3.03 [95% confidence interval = −6.20 to 0.15]). Figure 3 indicates that the effects of VR-based interventions on depression was not statistically significantly different, although the overall results favor the VR-based intervention (weighted mean difference of −1.11 [Z scores = 1.05, P =.29]). Figures 4 and 5 also show that the overall results favored VR-based intervention to reduce fatigue and pain levels, but only fatigue symptoms achieved statistical significance (Z score = 2.76, P = .006). Figure 6 and 7 indicate that the VR-based interventions had

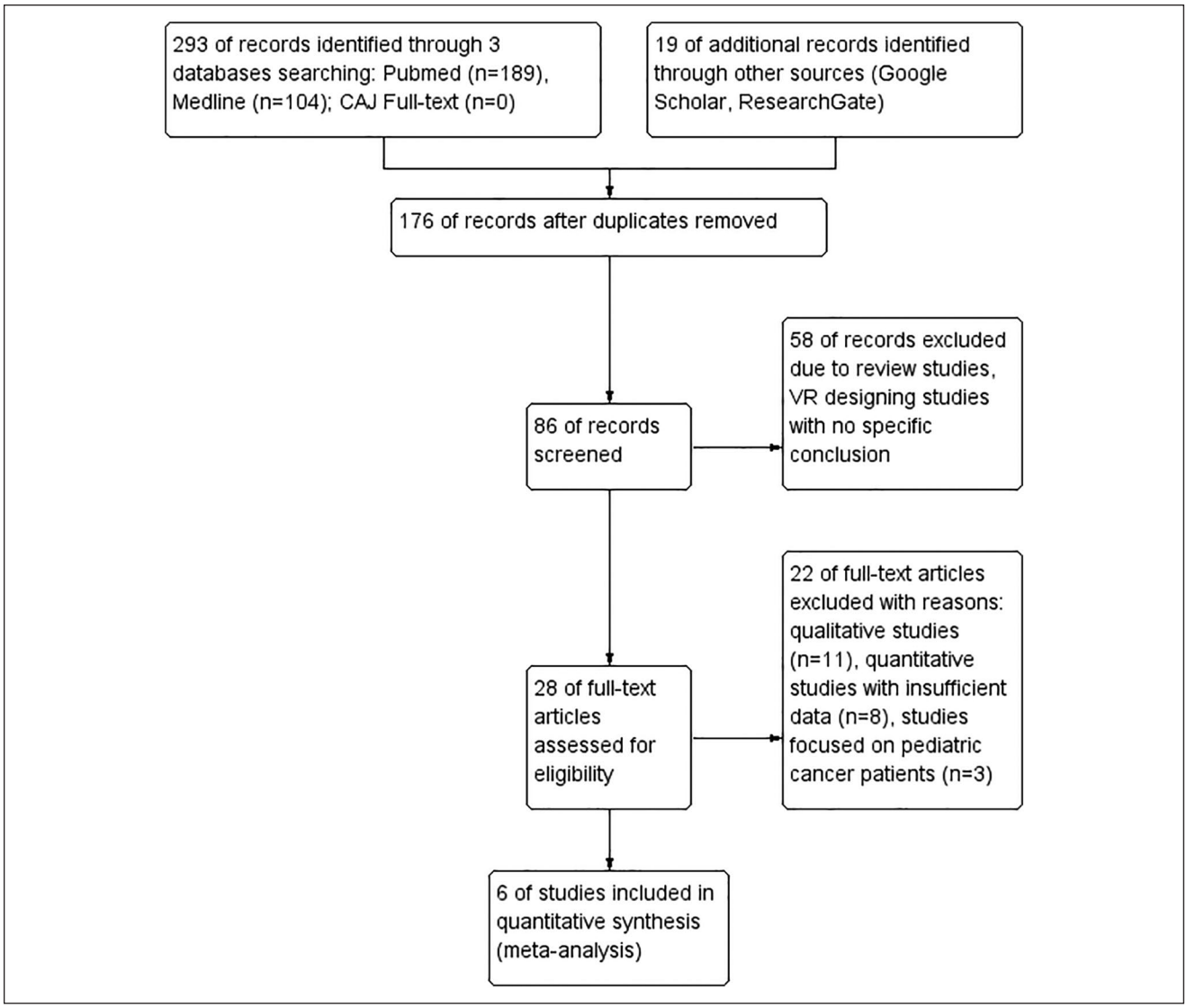

Figure 1. PRISMA flow diagram of study searching process.

favorable effects in improving cancer patients' cognitive function in verbal memory and processing speed, but there were no statistically significant differences (both $P > .05$).

Discussion

This updated meta-analysis synthesized the pooled effect of current VR-based interventions in cancer care. Consistent with previous research,[14] VR-based interventions improve cancer patients' emotional, cognitive, and physical well-being. Findings of this review indicate that VR-based interventions result in significant improvement in cancer-related symptoms of fatigue. This meta-analysis also found that other cancer-related symptom management issues, such as anxiety, depression, pain, and cognitive dysfunction, favor VR-based interventions, although there are no statistically significant differences, possibly due to the small sample sizes of the studies that were included.

Compared with traditional symptom-management interventions in cancer care, VR-based interventions, especially VR-based cognitive training, can allow cancer patients to learn. VR-based interventions offer instantaneous feedback on patient performance and then adjust the difficulty level to suit patient needs.[20,21] In addition, VR-based interventions incorporate the latest real-time graphics and imaging technology, allowing patients to experience numerous visual and auditory stimuli in a computer-generated virtual environment for their rehabilitative needs.[21] Most of the recent studies included in this meta-analysis applied VR-based interventions to patients in an acute stage of cancer care. As the management of late and long-term

Table 1. Characteristics of Included Studies.

Articles	Design	Study Sample	VR Methods	Intervention Duration	Outcomes/Instrument	Main Results
Baños et al[11] (2013)	Pre-post test	19 hospital inpatients diagnosed with metastatic cancer	Virtual environments were shown on a television connected to a computer, both were installed on a trolley that allowed movement from one room to another. A keyboard and mouse were used as interaction devices and participants used headphones.	A total of 4 sessions during 1 week. Half an hour per session.	VAS mood, physical discomfort, and satisfaction	There was significantly increasing positive emotions and decreasing negative emotions (all $P < .05$). There were other perceived benefits of distraction, entertainment, and promotion of relaxation states.
Hoffman et al[12] (2014)	Pre-post test	7 adult hospital patients were at least 21 years old with a diagnosis of lung cancer	VR exercise intervention: the home-based intervention promoted light-intensity, less than 3.0 metabolic equivalents, walking, and balance exercises utilizing an efficacy-enhancing VR approach using the Nintendo Wii Fit Plus.	A total of 16 weeks, walking with the Wii duration of 30 minutes per day for 5 days per week.	Brief Fatigue Inventory; Activities-Specific Balance Confidence Scale; Self-efficacy for Walking Duration Instrument	Subjects reported significantly improving the management of fatigue symptoms at the end of VR-based interventions ($P < .05$). Research participants also reported positive changes in perceived self-efficacy for walking at a light intensity continuously for 60 minutes.
House et al[18] (2016)	Pre-post test	6 community-dwelling women with postsurgical breast cancer pain in the upper arm	The VR-based rehabilitation system: a low-friction robotic rehabilitation table, a display, a laptop computer for the therapist station, a remote clinical server and a library of custom integrative rehabilitation games.	The duration of the VR-based therapy sessions progressed from 20 to 50 minutes of training over a period of 8 weeks, with 2 sessions every week.	BDI-II; BVMT-R; TMT-A; TMT-B; NAB; NPRS; HVLT-R; and PHQ-9	Pain intensity showed significant decreased ($P < .05$). Symptoms of depression decreased. Cognitive function improved posttraining.
Tsuda et al[19] (2016)	Pre-post test	16 hospitalized patients with hematologic malignancies aged more than 60 years	VR exercise using the Nintendo Wii Fit	20 minutes per session, once per day, 5 times a week, from the start of chemotherapy until hospital discharge.	Physical performance (eg, Barthel index, handgrip strength) and psychosocial performance (eg, HADS).	VR exercise using the Wii Fit may be feasible, safe, and efficacious, for patients with hematologic malignancies receiving chemotherapy.

(continued)

Table 1. (continued)

Articles	Design	Study Sample	VR Methods	Intervention Duration	Outcomes/Instrument	Main Results
Glennon et al[13] (2018)	CCT	97 adults in an outpatient cancer center. 49 participants were assigned to the experimental group (use of VR goggles) and 48 in the control group (standard treatment).	The use of ezVision X4 VR goggles and choosing among 3 relaxing nature scenes (ie, babbling brooks, swaying palm trees, or undersea life) that would then be projected through the goggles by a DVD.	Participants wore the goggles while lying in the prone position for the bone marrow aspiration and biopsy procedure. Relaxing music was heard through earphones built into the goggles. Duration of the procedure lasted, on average, 15 minutes.	NPRS; anxiety associated with the procedure was measured with a 5-item Likert-type scale.	Participants who wore VR goggles during a bone marrow aspiration and biopsy procedure showed a decrease in pain and anxiety levels from pre- to post-procedure.
Mohammad and Ahmad[17] (2018)	RCT	80 female patients with breast cancer at a specialized cancer center in Jordan.	Patients were randomized to either a VR scene or not scenarios including deep sea diving "Ocean Rift," or sitting on the beach with the "Happy Place" track by wearing a head mounted display with headphones.	One session of the immersive VR plus morphine injection.	SAI for anxiety and VAS for pain.	Patients randomized to receive immersive VR plus morphine reported a significant reduction in pain and anxiety, compared with morphine alone (all $P < .05$).

Abbreviations: BCS, breast cancer survivor; BDI-II, Beck Depression Inventory, Second Edition; BVMT-R, Brief Visuospatial Memory Test–Revised; CCT: case-controlled trial; CRF, cancer-related fatigue; DVD, digital versatile disk; HADS, Hospital Anxiety and Depression Scale; HVLT-R, Hopkins Verbal Learning Test–Revised; NAB, Neuropsychological Assessment Battery; NPRS, Numeric Pain Rating Scale; PHQ-9, Patient Health Questionnaire; RCT, randomized controlled trial; SAI, State Anxiety Inventory; STAI, State Trait Anxiety Inventory; TMT-A, Trail Making Test, Part A; TMT-B, Trail Making Test, Part B; VAS, Visual Analog Scale; VERT, virtual environment for radiotherapy training; VR, virtual reality.

Table 2. Design Quality Analysis.

Articles	Randomization	Control	Pre-Post Test	Retention	Missing Data	Power Analysis	Validity Measure	Follow-up	Scores
Banos et al[11]	−	−	+	+	−	−	+	−	3
Hoffman et al[12]	−	−	+	+	−	−	+	+	4
House et al[18]	−	−	+	+	−	−	+	+	4
Tsuda et al[19]	−	−	+	+	−	−	+	−	3
Glennon et al[13]	−	+	+	+	−	−	+	−	4
Mohammad and Ahmad[17]	+	+	+	+	+	+	+	−	7

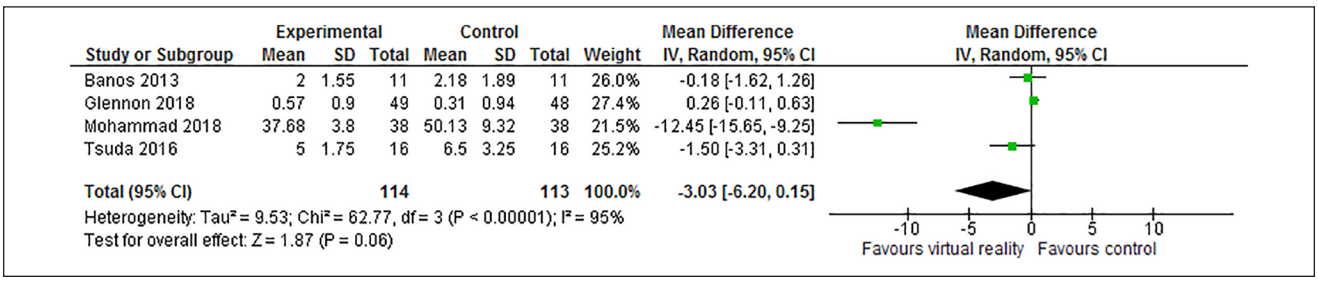

Figure 2. Anxiety after virtual reality–based intervention at post-intervention.

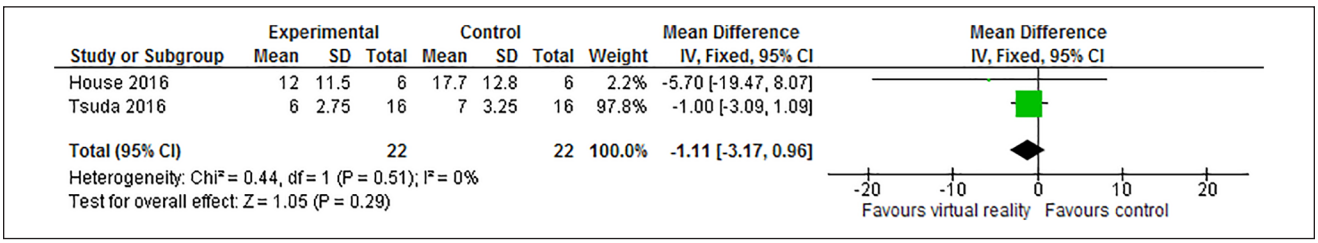

Figure 3. Depression after virtual reality–based intervention at post-intervention.

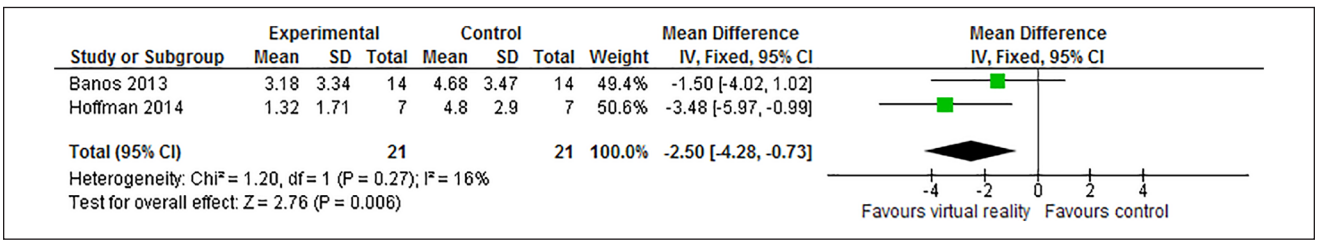

Figure 4. Fatigue after virtual reality–based intervention at post-intervention.

side-effects is central to cancer survivorship care, it will be important to examine the efficacy of this therapeutic modality for symptom management in cancer survivors.

This meta-analysis offers most updated quantitative evidence of efficacy for current VR-based interventions in cancer care. However, the interpretability and generalizability of the findings are limited by inclusion of a small number of studies given the novelty of this approach, generally small sample sizes, and heterogeneous study design (including data from single-arm studies). This meta-analysis excluded qualitative studies on cancer patients' experiences or perceptions of VR-based interventions in symptom

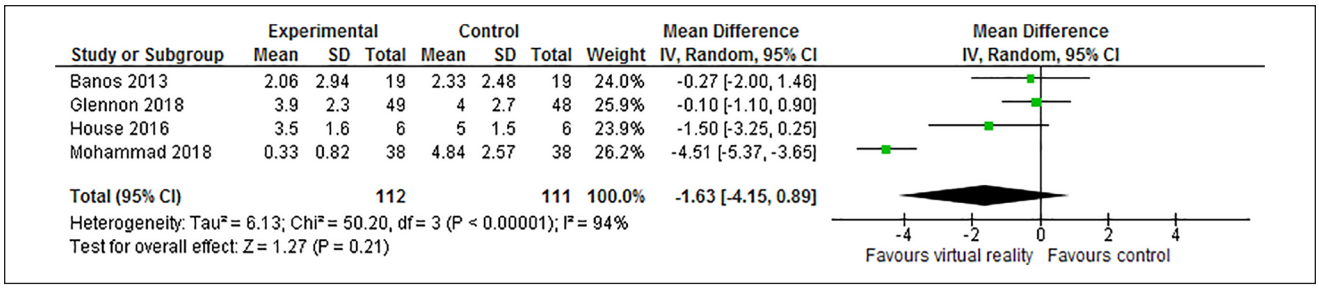

Figure 5. Pain after virtual reality–based intervention at post-intervention.

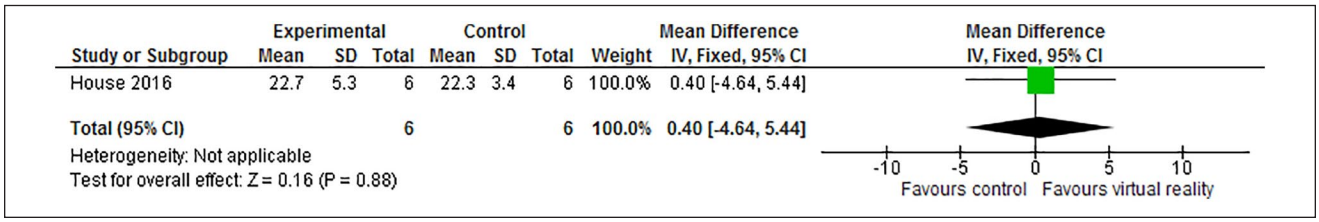

Figure 6. Cognitive function (ie, verbal memory) after virtual reality–based intervention at post-intervention.

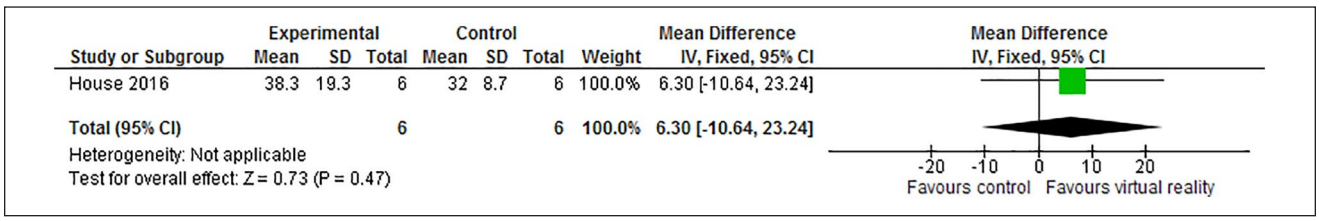

Figure 7. Cognitive function (ie, processing speed) after virtual reality–based intervention at post-intervention.

management, as these types of studies were beyond the aim of this review. Furthermore, the efficacy of VR-based interventions on cancer-related symptom management should be interpreted with caution. The studies that were included had relatively low methodological quality, indicating the need for studies with robust research design and sample size when conducting further investigations in this area. Last but not least, few of the studies included in this review evaluated the adverse effects of VR-based interventions, with a paucity of research assessing VR-related symptoms, such as the motion sickness effect.[11] This is an important issue, since VR is not without complications. Thus, future research is required to address these knowledge gaps, and long-term cancer survivors should be included as an additional target study population, in order to go beyond the acute stage of cancer symptom management.

Conclusion

This meta-analysis quantitatively pooled the effects of VR-based interventions in cancer-related symptom management. While the findings of this meta-analysis favor VR-based interventions, there is statistical significance only for the outcome of fatigue. Most recent studies have mainly applied VR-based interventions to the symptom management of patients in the acute stages of cancer care. However, the management of late and long-term side effects is central to cancer survivorship care. More research should be conducted to examine the efficacy of VR-based interventions in cancer rehabilitation. Future trials using this therapeutic modality would benefit from using randomized controlled trial designs, larger number of subjects, eligibility criteria that include presence of the symptom that is being treated, and longitudinal pre-post treatment designs.

Declaration of Conflicting Interests

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