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Virtual reality rehabilitation intervention for patients with Chronic Obstructive Pulmonary Disease: A systematic review and meta analysis of randomized controlled trials

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ADMINISTRATIVE INFORMATION

Support - None declared.

Review Stage at time of this submission - Data analysis.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 10 November 2023 and was last updated on 10 November 2023.

INTRODUCTION

Review question / Objective Chronic obstructive pulmonary disease (COPD) is an inflammatory lung disease characterized by irreversible blockage of airflow in the lungs. It is a major cause of chronic morbidity and mortality and constitutes a considerable economic and social burden throughout the world. The World Health Organization (WHO) predicts COPD to be the third leading cause of death worldwide by 2030. Pulmonary rehabilitation is a nonpharmacological intervention designed for patients with COPD, involving supervised exercise training, disease education, and behavioral interventions. It is now one of the most effective treatments for significantly improving symptoms of dyspnea (ie, breathlessness), exercise capacity, improved quality of life, and reducing anxiety and depression in patients with COPD. However, the

uptake of pulmonary rehabilitation is poor, and completion rates are low. Patients have difficulty attending classes because of lack of transport and geographic distance to a program, fatigue, lack of motivation, inconvenience, disruption caused to daily activities, and the quality of conversation that health care professionals have with patients about pulmonary rehabilitation. Therefore, researchers and practitioners are searching for innovative methods to deliver more engaging rehabilitation for patients with a variety of long-term conditions that affect physical activity.

More recently, there has been an increase in research focusing on the effects of virtual reality (VR) on patients with chronic diseases that inhibit physical activity. Virtual reality (VR) is a unique form of exercise established by Morton Heiling in 1962 and has been evolving over the past 60 years. VR technology is defined as a system that allows users to interact with images and sounds in a

virtual environment, which can stimulate response and provide real-time feedback concerning their performance. This technology can be combined with computer or mobile device screens and head-mounted displays to better interact with users.

Over the past decade, VR has gradually become a valuable tool for assessment and intervention in clinical rehabilitation due to the continuous research and cost reduction in the field of virtual technology. For example, studies focusing on individuals with Parkinson disease have investigated the effects of gait training with VR, whereas others have compared home-based VR balance training with conventional home-based balance training. However, despite the extant research in this area, studies investigating VR for physical training rehabilitation programs have demonstrated varying results, which means that researchers and practitioners are unsure about its true impact. The need for innovative methods of pulmonary rehabilitation is evident, and VR could be a promising technology for providing a convenient and remotely accessible pulmonary rehabilitation program to patients with COPD.

Remotely supervised VR could complement conventional therapy, which has demonstrated poor uptake because of patients' personal barriers. Therefore, we aimed to conduct a meta-analysis of randomized controlled trials (RCTs) through multiple literature searches to investigate the potential efficacy of VR rehabilitation intervention for patients with COPD.

Condition being studied Traditional programs of pulmonary rehabilitation have been shown to be capable of at least partially reversing muscle dysfunction and improving mobility; it is the most effective therapy to improve exercise tolerance in chronic respiratory diseases, idiopathic pulmonary fibrosis, and lung cancer. However, in international surveys, traditional pulmonary rehabilitation is available to only a small fraction of COPD patients. The need for innovative methods of pulmonary rehabilitation is evident. Alternate modes of rehabilitation are sought which might increase availability to patients who would benefit.

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VR could be a promising technology for providing a convenient and remotely accessible pulmonary

rehabilitation program to patients with COPD. However, studies investigating VR for physical training rehabilitation programs have demonstrated varying results, which means that researchers and practitioners are unsure about its true impact. We aim to re-evaluate the current research and update the VR rehabilitation compared to traditional rehabilitation in improving the effects of COPD patients.

METHODS

Participant or population The patients with Chronic Obstructive Pulmonary Disease.

Intervention Traditional pulmonary rehabilitation and virtual reality training.

Comparator Traditional pulmonary rehabilitation.

Study designs to be included Studies were included for RCTs reported in English or Chinese and published in a peer-reviewed journal.

Eligibility criteria The selection criteria were established according to the prespecified PICO strategy: (1) Participants: patients with COPD, irrespective of age and the stage of disease; (2) Interventions: unimodal intervention (VR therapy alone) or multimodal intervention (VR therapy in combination with other interventions), including various VR delivery device and levels of immersion. We define VR therapy as a technology that enables patients to interact with a virtual environment by motion sensors or other devices and receive real-time feedback to improve their performance; (3) Control: comparison with other interventions (eg, interventions without VR, standard treatment, no intervention); (4) Outcomes: the outcomes were pulmonary function (measured as the forced expiratory flow volume in one second [FEV1], or forced vital capacity [FVC], or the ratio FEV1/FVC), and functional capacity or aerobic capacity (measured as distance walked in six-minute walk test). Studies were excluded if they were nonrandomized controlled trials or quasi-RCTs, where quasi-randomized was considered as allocating patients based on a pseudorandom sequence (eg, admission number, date of birth, or alternate assignment). In addition, clinical observations, case reports, letters, abstracts, review articles, studies published in languages other than English and Chinese, and those with insufficient data after contacting the author were excluded from the final synthesis.

Information sources Databases utilized to search the eligible trials include 4 English literature

databases, namely, Medline (via PubMed), Embase, Web of Science Core Collection, Cochrane Library, as well as 3 Chinese literature databases, namely, China National Knowledge Infrastructure Library, Wan Fang database, and SinoMed databases. The databases were searched from their inception until October 2023. Relevant journals were manually searched to identify eligible studies. The last search was conducted on October 30, 2023.

The search was performed using a combination of relevant Medical Subject Headings (MeSH) terms and free text words: (Chronic Obstructive Pulmonary Disease or COPD or Chronic Obstructive or Pulmonary Disease) AND (virtual reality or virtual reality exposure therapy or VR or virtual reality simulator or virtual reality system or virtual reality head-mounted display or telerehabilitation or remote rehabilitation). Search strategies for each database are presented in Multimedia Appendix 1. After the selection stage, a further search was carried out by tracking the citations of the included trial (snowballing). The inclusion and exclusion criteria of studies were designed based on the PICO (Participants, Interventions, Control, and Outcomes) principle.

Main outcome(s) Exercise capacity measured by the distance walked in the six-minute walk test (6MWT) was descriptively presented as the primary outcome, pulmonary function described by the forced expiratory flow volume in one second (FEV1) or forced vital capacity (FVC) or the ratio FEV1/FVC as the secondary outcome, and the dyspnea evaluated on the MRC dyspnea scale or CAT scale or Borge scale.

Quality assessment / Risk of bias analysis Using the Cochrane Collaboration Risk of Bias Tool, the risk of bias was assessed as low risk, high risk, or unclear by two reviewers (MMX and JXZ) separately. We ranked risk based on the following seven domains: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other biases. Disagreements were resolved by discussion until a consensus was achieved. Data were imported into RevMan (version 5.3; Cochrane Collaboration) software to create the risk-of-bias plots.

Strategy of data synthesis The RevMan software was used to perform the statistical analysis and create forest plots to display the results. Related statistical indicators (mean, SD, and sample size) were extracted and imported into RevMan. Continuous outcomes were presented using mean

difference for outcomes measured using the same instrument, standardized mean difference (SMD) for outcomes measured by different methods, and 95% CIs. A fixed effects model was used to calculate the size of the pooled effect. When significant heterogeneity ($I^2 > 50\%$) was observed, the random effects model was used, and subgroup analysis was conducted to explore the possible causes of heterogeneity among the studies. Subgroup analyses were performed according to the comparisons of intervention (unimodal vs multimodal intervention), the control intervention, outcomes assessment, and type of population.

Subgroup analysis The Review Manager software (RevMan v.5.4.1) was used to summarize the effects of VR-Training on exercise capacity (6 Minute Walk Test-6MWT), subjective feeling of dyspnea (Borge scale or MRC scale or CAT scale), and pulmonary function (FEV1%). Subgroup analysis was performed for each outcome if there was clinical heterogeneity in the intervention and other details of studies, such as the population characteristics.

Sensitivity analysis Quantitative synthesis was carried out in accordance with the Cochrane Handbook for Systematic Reviews of Interventions guidelines, using the pre-post means and standard deviations from each chosen study for the between-group comparisons, either extracted directly from the articles or calculated where necessary. Since the studies employed the same outcomes for the reported comparisons, the mean difference (MD) and 95% confidence intervals (CI) were used. To determine the clinical relevance of the treatment for each outcome, a random-effects inverse variance model was chosen for meta-analysis. The I^2 statistic was used as a measure of heterogeneity, with values greater than 50% interpreted to indicate significant heterogeneity.

Country(ies) involved China.

Keywords virtual reality; rehabilitation; pulmonary disease, chronic obstructive; evidence-based nursing; meta analysis; systematic review.

Contributions of each author

Author 1 - MeiMei Xu - MeiMei Xu (first author) and MeiZhen Lin (corresponding author) were responsible for the study design.

Author 2 - JingXia Zheng - JingXia Zheng and LiJuan Zhang were responsible for the search strategy, study selection, and data extraction.

Author 3 - LiJuan Zhang - JingXia Zheng and LiJuan Zhang were responsible for the search strategy, study selection, and data extraction.

Author 4 - YaFang Zheng - YaFang Zheng, QiaoMei Wu, and QiuTing Wang carried out the literature assessment.

Author 5 - QiaoMei Wu - YaFang Zheng, QiaoMei Wu, and QiuTing Wang carried out the literature assessment.

Author 6 - QiuTing Wang - YaFang Zheng, QiaoMei Wu, and QiuTing Wang carried out the literature assessment.

Author 7 - XiaoZhen Gong - XiaoZhen Gong and JingMin Chen prepared and revised the manuscript.

Author 8 - JingMin Chen - XiaoZhen Gong and JingMin Chen prepared and revised the manuscript.

Author 9 - MeiZhen Lin - MeiMei Xu(first author) and MeiZhen Lin(corresponding author) were responsible for the study design.