INTRODUCTION

Review question / Objective: The present review will be a qualitative and quantitative analysis of current literature to assess the clinical effectiveness and safety of eccentric cycling in patients with COPD. The analysis carried out in this research will contribute by providing a theoretical and methodological training method for COPD patients. The study design is controlled clinical trial including randomized or non-randomized controlled trial.

Information sources: Literature research will be conducted in the eight electronic databases PubMed, The Cochrane Library, Web of Science, EMBASE, CNKI, VIP, CBM, and Wanfang database.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 16 January 2023 and was last updated on 16 January 2023 (registration number INPLASY202310048).

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Review Stage at time of this submission: Formal screening of search results against eligibility criteria.

Conflicts of interest: None declared.

The clinical effectiveness and safety of eccentric cycling for patients with COPD: A systematic review and meta-analysis

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**Condition being studied:** Chronic Obstructive Pulmonary Disease (COPD) are always characterized by persistent respiratory symptoms and airflow limitation due to airway and/or alveolar abnormalities, and the cause could be the significant exposure to harmful particulate matters. According to 2019 World Health Organization (WHO) "Global Health Assessment", COPD is the top three disease of a global cause of death. The results showed that In 2019, 212.3 million COPD epidemic cases were reported globally, with COPD causing 3.3 million deaths. By 2060, it is estimated that more than 5.4 million people will die of COPD and its related diseases every year. Once suffering from COPD, not only the patients' quality of life decreases, but also the cost of yearly medication and oxygen therapy is enormous, bringing a heavy burden to the family and society. It was reported that COPD will become the top 5 burden disease in the world by 2030. Therefore, scientific prevention and effective treatment is particularly important. 2022 gold COPD guidelines state that as an important adjuvant means to treat COPD, pulmonary rehabilitation training refers to individualized, multi-course and comprehensive intervention measures which can reduce the burden of symptoms and improve cardiovascular function. Exercise training is one of the most important components of any pulmonary rehabilitation program. The role of exercise as a therapeutic tool is central to the concept of pulmonary rehabilitation, which not only improves functional dyspnea and health-related quality of life, but has also been shown to enhance exercise capacity in COPD patients. International guidelines recommend that the exercise component of PR includes both aerobic and resistance training.

**METHODS**

**Participant or population:** Adult men and women, i.e. individuals from 18 years of age and upwards, with moderate or severe COPD. Inclusion criteria: 1. ratio of forced expiratory volume in 1 s (FEV1) over forced vital capacity (FVC) < 70 %, and FEV1 < 80 % of predicted value according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria. 2. choose level B, C and D in the comprehensive assessment system for stable COPD patients. Exclusion criteria: unstable angina pectoris; severe arrhythmia; cardiac insufficiency; uncontrolled hypertension; neuromuscular disorders, arthropathies, peripheral vascular diseases that affect exercise, etc; severe cognitive or psychiatric disorders, etc.

**Intervention:** Eccentric cycling with or without usual care (e.g. respiratory rehabilitation training and/or medical treatment). Usual exercise includes resistance exercise and non resistance exercise. The eccentric cycling interventions need to performed on a cycle ergometer in which motor powered pedals are moved backward so that both exercise and execution will be clearly identified and so that the eccentric loading will be easily compared with any control.

**Comparator:** Concentric cycling and with or without usual care (e.g. respiratory rehabilitation training and/or medical treatment). The usual care of the control group and the intervention group must be consistent.

**Study designs to be included:** controlled clinical trial including randomized or non-randomized controlled trial. We will include parallel, cross-over and before-after controlled trial.

**Eligibility criteria:** After removing duplication, two reviewers will independently screen titles, abstracts, and full texts. Any differences will be settled through consultation between two reviewers (Zhou mc and Zhou mq). We will record the exclusion reasons of the full text. After removing duplication, two reviewers will independently screen titles, abstracts, and full texts. Any differences will be settled through consultation between two reviewers (Zhou mc and Zhou mq). We
recorded the exclusion reasons of the full text. Literature research will be conducted in the eight electronic databases PubMed, The Cochrane Library, Web of Science, EMBASE, CNKI, VIP, CBM, and Wanfang database.

Information sources: Literature research will be conducted in the eight electronic databases PubMed, The Cochrane Library, Web of Science, EMBASE, CNKI, VIP, CBM, and Wanfang database.

Main outcome(s): FEV1/FVC (% of predicted post-bronchodilator) and FEV1 (% of predicted post-bronchodilator).

Additional outcome(s): heart rate, dyspnea, muscle strength, six-minute walk test, the quadriceps muscle isometric peak torque, MVC strength, muscle soreness, plasma CK activity, rating of perceived exertion, oxygen consumption, minute ventilation, leg fatigue, breathing frequency.

Quality assessment / Risk of bias analysis: The risk of bias will be independently evaluated by two reviewers (Zhou mc and Zhou mq) using the Cochrane Collaboration Bias Risk Assessment tool. Any difference will be reevaluated by a third reviewer (Chen x). Each study will be rated as low-, high- or unclear-risk in terms of random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other bias. If there are still any differences, the third researcher arbitrates (Li X).

Strategy of data synthesis: This meta-analysis will be performed using Review Manager Software 5.4. The weighted mean difference will be used as the effect size for the continuous variables. The standardized mean difference will be used if the data are not consistent in units. Risk ratios (RR) will be presented if the results are binary variables. The 95% CI and p-value will be calculated for each effect size.

Subgroup analysis: subgroup1: higher ECC vs CON training intensity

Sensitivity analysis: If there is obvious clinical or methodological heterogeneity, random-effect model will be applied, otherwise we will apply fixed-effect model if I² < 50%. We will further perform a sensitivity analysis to assess the robustness of the results. Funnel plots will be used to assess potential publication bias if the number of trials for one meta-analysis is more than 10.

Country(ies) involved: China.

Keywords: Eccentric cycling, Chronic obstructive pulmonary disease (COPD), Meta-analysis, Systematic review.

Contributions of each author: Author 1 - Man-ci Zhou. Author 2 - Meng-qing Zhou. Author 3 - Xu Chen. Author 4 - Xun Li.