INPLASY

Effects of beta-blocker withdrawal in patients with heart failure with preserved ejection fraction: a protocol for systematic review and meta-analysis

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Preliminary searches.

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 17 July 2023 and was last updated on 17 July 2023.

INTRODUCTION

Review question / Objective Nearly half of patients with heart failure in the community have preserved ejection fraction (EF). The primary chronic symptom of patients with heart failure with preserved EF (HFpEF) is severe exercise intolerance. The inability to adequately increase heart rate during exercise (chronotropic incompetence) is commonly present in HFpEF patients and contributes importantly to exercise intolerance in these patients.

Since HFpEF patients are likely to have cardiac comorbidities such as hypertension, coronary artery disease (CAD), and atrial fibrillation (AF), beta-blockers are commonly used in these patients. However, there is no definitive evidence regarding the use of beta-blockers in HFpEF patients. Furthermore, there is a concern that beta-blockers may worsen chronotropic incompetence by slowing heart rate in HFpEF patients and may further exacerbate their symptoms. There are several studies on the effects of beta-blocker withdrawal in HFpEF patients. To gain a better understanding of how beta-blocker discontinuation affects outcomes in HFpEF patients, we aim to perform the meta-analysis of studies on the effects of beta-blocker withdrawal in these patients.

Condition being studied Stable patients with heart failure with preserved ejection fraction.

METHODS

Participant or population Patients with heart failure with preserved ejection fraction treated with beta-blockers.

Intervention Beta-blocker withdrawal.

Comparator Beta-blocker continuation.

Study designs to be included Randomized controlled trial and prospective cohort studies.

Eligibility criteria Inclusion criteria for this meta-analysis included: (1) included HFpEF patients treated with beta-blockers; (2) compared between

beta-blocker withdrawal and beta-blocker continuation; and (3) assessed exercise capacity, health-related quality of life, plasma B-type natriuretic peptide (BNP) levels, or cardiac structure and function.

Information sources PubMed, Web of Science, and Scopus.

Main outcome(s) The primary outcome will be exercise capacity. In the measures of exercise capacity, peak oxygen uptake (peak VO2) and 6-minute walk distance will be extracted.

Additional outcome(s) The secondary outcomes will be health-related quality of life. Other outcomes of interest will be plasma B-type natriuretic peptide (BNP) levels and cardiac structure and function. In the measures of cardiac structure, LV mass and left atrial volume will be extracted. In the measures of LV systolic function, LV ejection fraction and early systolic mitral annular velocity (s') will be extracted. In the measures of LV diastolic function, early diastolic mitral annular velocity (e') and the ratio of early diastolic mitral inflow to annular velocities (E/e') will be extracted given the linear relationship with LV diastolic dysfunction grade.

Quality assessment / Risk of bias analysis The Cochrane Risk of Bias tool will be used to assess quality of RCTs. The quality of prospective cohort studies will be evaluated by Newcastle-Ottawa Scale tool.

Strategy of data synthesis The effect size for the intervention will be calculated by the difference between the means of the intervention and control groups at the end of the intervention. If the outcome is measured on the same scale, the weighted mean difference and 95% confidence interval (CI) will be calculated. Otherwise, the standardized mean difference and 95% CI will be calculated. For each outcome, heterogeneity will be assessed using the Cochran's Q and I2 statistic; for the Cochran's Q and I2 statistic, a p value of 50%, will be considered significant, respectively. When there is significant heterogeneity, the data will be pooled using a random-effects model, otherwise a fixed-effects model will be used. When there are more than 10 studies included, publication bias will be assessed graphically using a funnel plot and mathematically using Egger test. For these analyses, Comprehensive Meta Analysis Software version 2 (Biostat, Englewood, NJ, USA) and STATA 16 software (Stata Corp LP, TX, USA) will be used.

Subgroup analysis Subgroup analysis stratified by study design (RCT or prospective cohort study) will be performed.

Sensitivity analysis Meta-regression will be used to determine whether the effect of beta-blocker withdrawal will be confounded by baseline clinical characteristics such as age, sex, New York Heart Association functional class, atrial fibrillation, and coronary artery disease.

Country(ies) involved Japan.

Keywords Heart failure; Beta-blockers; Withdrawal; Systematic Review; Meta-analysis.

Contributions of each author

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