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### ADMINISTRATIVE INFORMATION

**Support** - None.

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

**Conflicts of interest** - None declared.

**INPLASY registration number:** INPLASY202380116

**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 28 August 2023 and was last updated on 28 August 2023.

### INTRODUCTION

**Review question / Objective** Ischemic mitral regurgitation (MR) is associated with a poor prognosis. We aimed to compare the safety and efficacy of current available interventions in the management of ischemic MR.

**Condition being studied** Patients with chronic coronary artery lesions often occurs left ventricular dilation and remodeling, which leads to mitral complex incompetence, ultimately resulting in ischemic mitral regurgitation (IMR). The grade of IMR achieves moderate or severe is a sign of advanced coronary diseases, and is associated with a poor long-term survival. Currently, surgical strategies for mitral valve consist of annuloplasty, valve replacement, annuloplasty plus subvalvular repair, and no intervention; however, the optimal choice remains controversial.

### METHODS

**Search strategy** Combination of the following keywords: “ischemic or ischaemic or functional”, “mitral regurgitation or mitral incompetence”, “randomized or randomised or propensity”.

**Participant or population** Patients with ischemia mitral regurgitation.

**Intervention** Various mitral interventions.

**Comparator** Various mitral interventions.

**Study designs to be included** Randomized controlled study and high-quality propensity score matched (PSM) observational study.

**Eligibility criteria** 1. study design was RCT or PSM; 2. including the primary endpoint; 3. diagnosed as MR.

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**Information sources** Electronic databases including PubMed, Web of Science, and the Cochrane Central Register of Controlled Trials was systematically searched from the date of their inception to June 2023.

**Main outcome(s)** The primary endpoints were early (within 30 days or in-hospital period) and late (at 5 years) all-cause mortality. The secondary outcomes comprised heart failure (HF) rehospitalization, mitral valve (MV) reoperation, and recurrent moderate or severe MR (grade 3+).

**Quality assessment / Risk of bias analysis** The methodological quality of RCTs and PSM studies were evaluated by the Jadad scale and the Newcastle-Ottawa score (NOS), respectively. The Jadad score ranges from 0 to 5 points and NOS ranges from 0 to 9 points. The studies were considered to be of high quality if the Jadad score  $\geq 3$  or NOS  $\geq 6$ .

**Strategy of data synthesis** Direct pairwise meta-analysis was performed for different studies with similar interventions. We calculated odds ratio (OR) and corresponding 95% confidence intervals (CI) using the Mantel-Haenszel method with a random-effects model. The heterogeneity of pooled results was quantitatively assessed with  $I^2$  and chi-square tests. Funnel plots were not drawn for estimating the risk of publication bias due to there were fewer than 10 studies.

We conducted a network meta-analysis with a random-effects model using the Markov-Chain Monte Carlo (MCMC) simulations under a Bayesian framework. For each outcome, we generated a consistency model on the computer with 4 chains, while the number of tuning iterations and simulation iterations in each chain was set at 20000 and 50000, respectively. Convergency of the MCMC model was evaluated using the Brooks-Gelman-Rubin method, which compares within-chain and between-chain variance to calculate the potential scale reduction factor (PSRF). A PSRF close to 1.0 indicates approximate convergence has been reached. We used forest plot to show the comparisons of different interventions; furthermore, a rank probability plot was applied to display the calculated treatment ranks. Rank 1 is considered as the highest likelihood leading to the relevant outcome, whereas rank N is associated with the most unlikely. In addition, we also used the surface under the cumulative ranking curve (SUCRA) metric to rank the effectiveness of each treatment and identify the “best” treatment. Inconsistency could not be evaluated, because there is not existing a loop in the present network.

**Subgroup analysis** None.

**Sensitivity analysis** None.

**Country(ies) involved** China.

**Keywords** ischemia mitral regurgitation, interventions, network meta-analysis.

#### **Contributions of each author**

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Author 2 - Xiaohan Zhong.

Author 3 - Chuang Liu.

Author 4 - Yuyong Liu.

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