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Letter to the Editor

Mitral valve replacement therapy causes higher 30-day postoperative mortality than mitral valvuloplasty in patients with severe ischemic mitral regurgitation: A meta-analysis of 12 studies

Jiayang Wang, Chengxiong Gu, Mingxin Gao, Wenyuan Yu, Yang Yu *

Department of Cardiac Surgery, Beijing An Zhen Hospital, Capital Medical University, Beijing 100029, China

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Percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG) usually can achieve satisfactory revascularization in patients with ischemic heart diseases. However, for patients with combined ischemic mitral regurgitation (IMR), particularly with severe IMR, the outcomes of PCI and CABG are poor and postoperative mortality is high [1]. The cause of IMR is associated with myocardial injury-induced adverse remodeling of the left ventricle [2]. Patients with IMR often exhibit enlarged left ventricular chamber and mitral annulus, apical and lateral migration of the papillary muscles, and leaflet tethering [2]. The closing force of the mitral valve is substantially reduced [2]. The complex pathophysiological characteristics of IMR increase surgical risks in patients undergoing combined CABG and mitral valve surgery [3]. Thus, mitral valve surgery simultaneous to coronary revascularization is still a controversy [4]. The latest guidelines from the American College of Cardiology/American Heart Association, the European Society of Cardiology and the European Association for Cardio-Thoracic Surgery recommend mitral valve surgery for patients with severe IMR [5,6]. However, a specific type of mitral valve surgery is not indicated in the guidelines. The differences in patient outcomes of mitral valve replacement versus repair remain inconclusive. The aim of this meta-analysis was to compare the 30-day postoperative survival rate in patients with IMR undergoing mitral valvuloplasty (MVP) versus mitral valve replacement (MVR) and determine the optimal procedure for severe IMR.

Two investigators searched the literature databases PubMed, Ovid, and Elsevier for English reports published before March 2014 separately. All the articles investigating patients with mild/moderate/severe IMR undergoing MVR or MVP with CABG were collected and the full text reports were screened. The articles reporting the risk of 30-day postoperative mortality in patients undergoing MVR or MVP with CABG were selected for meta-analysis. Duplication of previous publication, articles in the format of abstract, review, comments, or editorial, and studies including MVP without using annuloplasty ring were excluded. The endpoint was 30-day postoperative mortality rate. The odds ratio (OR) with a 95% confidence interval (95% CI) of the predetermined end point was determined. The I^2 index was calculated to estimate the study heterogeneity with > 50% indicating significant heterogeneity. Sensitivity analysis was conducted to evaluate the effects of each individual report on the overall results. Funnel plot and Egger's weighted regression test were used to assess publication bias. All the data were analyzed using the statistical analysis software STATA. P value was 2 sided and $P < 0.05$ was considered statistically significant.

In total, 12 articles including 2936 patients were selected for meta-analysis (Table 1) [2,7–17]. No study heterogeneity was detected ($I^2 = 0.0\%$, $P = 0.460$). Reports including subgroup patients with severe IMR did not show significant heterogeneity either ($I^2 = 0.0\%$, $P = 0.634$). Thus, a fixed-effects model was used. Sensitivity analysis revealed no impacts of each individual study on the overall result (Fig. 1). The results of meta-analysis demonstrated that 30-day postoperative mortality in patients undergoing MVR was significantly increased compared with that in patients undergoing MVP (OR = 2.52, 95% CI = 1.91–3.34, Z = 6.46, $P = 0.000$, Fig. 2). In the subgroup patients with severe IMR, the mortality rate associated with MVR was 3.27 times that associated with MVP (OR = 3.27, 95% CI = 1.21–8.84, Z = 2.33, $P = 0.02$, Fig. 3). Both the funnel plot (Fig. 4) and Egger's weighted regression test find no significant publication bias ($P = 0.365$).

Selection between MVR and MVP for patients with IMR is always controversial due to the lack of evidence to support the superiority of either approach [2]. De Bonis et al. found that patients with advanced dilated and ischemic cardiomyopathy and severe functional MR showed higher in-hospital and late mortality when undergoing MVR compared with patients with similar condition undergoing MVP [16]. Thus, mitral

* Corresponding author.
E-mail address: heartyuyang@hotmail.com (Y. Yu).

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Table 1
Characteristics of included studies (n = 12).

Author	Year	Study design	Study size	Surgical procedures and patients characteristics
Hickey	1988	OB	59	Patients undergoing valve replacement or repair in addition to coronary bypass for moderate and severe IMR
Gillinov	2001	OB	482	Patients undergoing either mitral valve repair or replacement for IMR
Mantovani	2004	OB	102	Patients with a preoperative diagnosis of CIMR, underwent mitral valve repair or prosthetic replacement, along with myocardial revascularization
Reece	2004	OB	110	Patients undergoing CABG and MVP or MVR for IMR
Al-Radi	2005	OB	202	Patients with IMR undergoing repair or replacement
Silberman	2006	OB	80	Patients with severely impaired LV function (ejection fraction < 25%) and severe IMR
Milano	2008	OB	522	Patients undergoing CABG and MVP or MVR for IMR
Micovic	2008	OB	138	Patients with IMR undergoing either MVR or MVP
Magne	2009	OB	370	Patients with CIMR who underwent mitral valve surgery
Bonis	2012	OB	132	Patients with advanced dilated and ischemic cardiomyopathy and severe functional MR and systolic dysfunction underwent mitral surgery in the same time frame.
Lorusso	2013	OB	488	Patients with CIMR and LV ejection fraction (LVEF) < 40% undergoing CABG procedure associated with MVP with downsizing ring annuloplasty or MVR.
Acker	2014	RCT	251	Patients with severe IMR undergoing either MVR or MVP

repair appeared to be an optimal option for patients with severe IMR [16]. In contrast, Acker et al. reported that the clinical outcomes of MVP and MVR were not significantly different, while MVR seemed to show better and more sustained efficacy than MVP in patients with MR [2]. In this report with a large number of patients, we compared 30-day postoperative mortality in patients receiving mitral valve repair versus replacement therapy and found that the mortality associated with MVR was 2.52 times that associated with MVP, which is consistent with the results from a previous meta-analysis [18]. This result was from the analysis of all the patients with various degrees of severity of IMR. In clinical practice, MVR is usually performed on patients with moderate–severe IMR, while patients with mild–moderate IMR often undergo MVP although the benefits of simultaneous mitral valve surgery to CABG in those patients are still uncertain [19]. Thus, the poor short-term outcome in patients undergoing MVR might be attributable to patient's condition but not the mitral valve surgery. To accurately compare the clinical outcome of the 2 procedures, we performed the subgroup analysis on patients with severe IMR. To our knowledge, this is the first meta-analysis to compare the short-term outcomes of mitral valve procedures on patients with severe IMR. Our results show that in this subgroup, the 30-day postoperative mortality in patients undergoing MVR was 3.27 times that in patients undergoing MVP. The study heterogeneity was minimal in this analysis. These findings suggest that compared with MRP, MVR in patients with IMR, particularly with severe IMR, causes poorer short-term clinical outcomes.

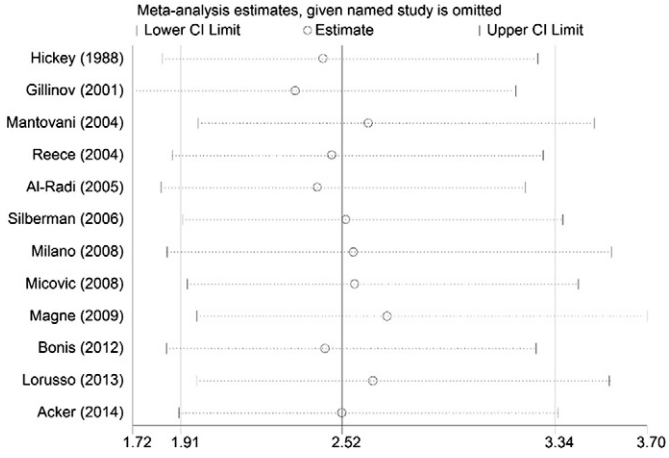

Fig. 1. Sensitivity analysis of the included studies.

Multiple reasons might contribute to the advantage of MVP in short-term clinical outcomes over MVR in patients with severe IMR. A tethered loop formed by mitral valve, myocardial fibers, anterior and posterior papillary muscle, chordae tendineae, and leaflets stabilizes the left ventricle and plays a critical role in left ventricular contraction [20]. Although MVR can sufficiently correct MR, the structural integrity of the mitral valve is usually compromised after MVR, leading to a continuous damage on the left ventricular tethered loop, which results in adverse effects on left ventricular contraction and poor prognosis. Contrarily, in MVP, the structure of mitral valve is preserved so that the structure and function of left ventricle remain intact [12]. In addition, anticoagulant therapy after MVR frequently causes serious complications such as thrombosis and bleeding, which further hamper postoperative recovery in patients with severe IMR [18]. Despite the fact that a better short-term outcome of MVP than MVR was observed in this study, problems and challenges associated with MVP should not be overlooked. In our practice, we find that the efficacy of MVP is uncertain. Many patients still develop regurgitation after MVP. Severe recurrent regurgitation after MVP damages left ventricular function and increases surgical mortality. The complex surgical procedure of MVP places high demands on surgeon's surgical techniques and skills. Therefore, to develop an optimal therapeutic strategy for patients with IMR, we recommend adequately evaluating the patient's condition and the severity of MR by echocardiography and ventricular angiography before operation. Furthermore, determining a proper annuloplasty ring for MVP is also challenging for cardiac surgeons. Conventional undersized annuloplasty rings can sufficiently reduce mitral septal-to-lateral dimension, but they raise the risk of relative mitral stenosis [21]. The emergence of annuloplasty rings designed for specific valvular diseases further complicate the selection. Bothe et al. compared the measured dimensions of 4 new disease-specific rings versus a standard ring and found that 3 of the 4 rings actually had a larger septal-to-lateral dimension than the standard ring [22]. On the other hand, the report by De Bonis et al. suggests that disease-specific rings might not reduce recurrent MR compared with standard rings [23]. Thus, evidence to support the superiority of disease-specific rings to standard rings is still lacking. We believe that mitral valve annuloplasty still needs to be improved and that comprehensive prospective studies are required to clarify whether mitral valve annuloplasty can reduce recurrent MR and prompt left ventricular reverse remodeling effectively.

The limitations of this study are that the meta-analysis was mostly based on observational studies with only 1 randomized control trial and that the number of patients with severe IMR in the analysis was relatively small. Large-scale studies are required to further verify the conclusion.