Similar Survival After Mitral Valve Replacement or Repair for Ischemic Mitral Regurgitation: A Meta-Analysis

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Background. Ischemic mitral regurgitation (IMR) occurs in 20% of patients after myocardial infarction [1]. There is no agreement as to the best surgical option. With no prospective randomized controlled trials available, our objective was to perform a meta-analysis comparing replacement and repair.

Methods. A literature search was performed in PubMed, EMBASE, Ovid, and Google Scholar. The following keywords were included: “ischemic mitral regurgitation” and “repair or replacement.” Inclusion and exclusion criteria were used to reflect current surgical practice (subvalvular preservation, ring annuloplasty). Primary outcomes of interest were operative mortality and survival. Secondary outcomes analyzed were change in ejection fraction (EF), left ventricular (LV) dimensions, New York Heart Association (NYHA) class, reoperation rate, and 2+ or greater recurrence of mitral regurgitation.

Results. Of 280 articles, only 12 satisfied all inclusion and exclusion criteria. These articles included 2,508 patients, 64% of whom received valve replacement. Operative mortality was lower after repair (odds ratio [OR], 0.56; 95% confidence interval [CI], 0.38–0.85; \( p = 0.001 \)); no difference was found when only articles with patients operated on mainly after 1998 were included (OR, 0.70; 95% CI, 0.44 –1.12; \( p = 0.14 \)). Survival was similar [hazard ratio (HR), 0.86; 95% CI, 0.66–1.13; \( p = 0.28 \)]. No differences were found in EF, ventricular dimensions, NYHA class, and reoperation were found. Regurgitation recurrence was higher in the repair group (OR, 7.51; 95% CI, 3.7–15.23; \( p < 0.001 \)).

Conclusions. Mitral valve repair is associated with lower operative mortality but higher recurrence of regurgitation in patients with ischemic mitral regurgitation. No differences were found regarding survival, NYHA class, and functional indicators.


Ischemic mitral regurgitation (IMR) is present in 20% to 30% of patients after an acute myocardial infarction [1]. When IMR is severe, survival can be as low as 60% at 1 year [2].

Patient survival after operation for IMR is worse than for organic MR [3]. Patients with IMR and coronary artery disease who undergo isolated coronary artery bypass grafting have worse survival, and MR persists in these patients [4]. Current guidelines consider surgical intervention for IMR with an ejection fraction (EF) 30% or greater as a class I recommendation; a class IIb recommendation is when the EF is 30% or less [5].

The durability of repair of degenerative MR over the long term is well established [6], but recurrence of functional MR is common because of the progressive nature of the underlying ventricular disease (30%–40% annually) [7]. The best operation for IMR is controversial. Some studies recommend repair [8, 9], others replacement [10], and others show no differences because both options had the same outcomes [11].

Previous meta-analyses concluded that mitral valve repair (MVP) is associated with better short- and long-term survival when compared with mitral valve replacement (MVR) [12]. There are no prospective randomized trials comparing MVP with MVR in patients with chronic IMR. Until the results of an ongoing trial are available [13], meta-analysis is the only tool to evaluate the accumulated evidence. The purpose of this study was to perform a meta-analysis of the available evidence of the best operative option for IMR.

Material and Methods

A literature search was performed in PubMed, EMBASE, Ovid, and Google Scholar for studies published between 1965 and 2013 without language restriction according to the following criteria: exp *Mitral Valve Insufficiency/or ischemic mitral regurgitation.mp. or exp *Ventricular Dysfunction, Left/or Mitral Valve Insufficiency/su [Surgery] or exp *Ventricular Dysfunction, Left/or...
Table 1. Demographics of Patients in Included Studies

<table>
<thead>
<tr>
<th>Patients</th>
<th>Age</th>
<th>Female (%)</th>
<th>HTN</th>
<th>Diabetes</th>
<th>COPD</th>
<th>NYHA III-IV</th>
<th>RF</th>
<th>Emergency</th>
<th>Recent AMI</th>
<th>LVEF</th>
<th>Era of Operation</th>
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<td>56</td>
<td>65.5</td>
<td>68.6*</td>
<td>45</td>
<td>52</td>
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<td>NS</td>
<td>NS</td>
<td>89</td>
<td>98</td>
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<tr>
<td>Mantovani et al [20]</td>
<td>61</td>
<td>41</td>
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<td>NS</td>
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<td>NS</td>
<td>NS</td>
<td>22</td>
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<td>15</td>
<td>NS</td>
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<tr>
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<td>14</td>
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<td>67</td>
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<td>Maltais et al [17]</td>
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<td>70</td>
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*p < 0.05 between MVP and MVR. A and B after surgical era represent their inclusion in the analysis as either after or before 1998.

AMI = acute myocardial infarction; COPD = chronic obstructive pulmonary disease; HTN = hypertension; LVEF = left ventricular ejection fraction; MVP = mitral valve repair; MVR = mitral valve replacement; NS = not significant.
or after 1998) based on the time frame in which the study patients were included. For example, articles in which patients were operated on between 1995 and 2005 would be assigned to the “after 1998 era” because most of the patients were operated on after 1998 (a similar number of patients per year was assumed). Values of $p$ less than 0.05 were considered significant. Funnel plots were inspected to assess the potential of publication bias. Meta-analysis results are displayed in forest plots. Analysis was conducted using Review Manager, version 5.2 (The Cochrane Collaboration, Update Software, Oxford).

### Results

Two hundred eighty studies published between 1965 and 2013 were identified. On the basis of title and abstracts, 36 articles were selected and reviewed in full. Twelve articles met the inclusion and exclusion criteria [8–11, 17–24]. All were retrospective and nonrandomized studies. They included a total of 2,509 patients, 1611 (64%) of whom underwent MVP. Patient characteristics in eligible studies and procedures performed are summarized in Tables 1 and 2, respectively.

#### Hospital Mortality

A total of 11 studies (2,416 patients) reported hospital mortality (Fig 1A). ORs ranged from 2.32 (favoring replacement) [17] to 0.16 (favoring repair) [18]. The summary OR was 0.56 (95% CI, 0.38–0.85; $p = 0.001$). Studies in which patients were operated on mainly after 1998 [11, 17, 19–23] had an OR of 0.70 (95% CI, 0.44–1.22; $p = 0.14$) (Fig 1B), whereas the remaining studies had an OR of

<table>
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<th>Table 2. Procedures Performed in Included Studies</th>
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<tr>
<td><strong>MVR Prosthesis (%)</strong></td>
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<tr>
<td>Mechanical</td>
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<tr>
<td>Cohn et al [10]</td>
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<tr>
<td>Mantovani et al [20]</td>
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<td>Silberman et al [9]</td>
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<td>Milano et al [8]</td>
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<td>Magne et al [22]</td>
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<td>Qiu et al [21]</td>
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<td>Maltais et al [17]</td>
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<td>Lorusso et al [11]</td>
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<td>Chan et al [23]</td>
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**CEAS** = Crosgrove-Edwards annuloplasty system; **CEC** = Carpentier Edwards Classic; **CEMc** = Carpentier Edwards McCarthy ETlogix; **CEP** = Carpentier Edwards Physio; **CEPII** = Carpentier Edwards Physio II; **DA** = Duran AnCore; **Geo** = St Jude Geoform; **MF** = Medtronic Future Band; **MVP** = mitral valve repair; **MVR** = mitral valve replacement.
of 0.41 (95% CI, 0.25–0.68; \( p < 0.001 \)). When both results were compared using a z test, no differences were found (\( p = 0.16 \)).

**Survival**

Eleven studies reported long-term survival (Fig 2A). The study HR was 0.86 (95% CI, 0.66–1.13; \( p = 0.28 \)). Heterogeneity was moderate (I\(^2\) = 65%). To explain heterogeneity, subgroup analysis was performed based on surgical era and propensity-matched studies. Only 4 studies included propensity-matched patients [11, 17, 22, 23]. When only these studies were included, heterogeneity was null (I\(^2\) = 0%); and the pooled HR was 1.05 (95% CI, 0.92–1.19; \( p = 0.46 \)) (Fig 2B). Subgroup analysis based on surgical era (with patients operated on mainly after 1998) revealed low heterogeneity (I\(^2\) = 0%) [11, 17, 19–22]. After meta-regression including surgical era and propensity matches as covariates, only surgical era resulted as a

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**Fig 1.** Operative mortality forest plots. (A) Global mortality: OR = 0.56 (95% CI, 0.38–0.85; \( p = 0.006 \)). (B) Including only articles in which patients were operated on mainly after 1998: OR = 0.7 (95% CI, 0.44–1.12; \( p = 0.14 \)). (CI = confidence interval; df = degrees of freedom; M-H = Mantel-Haenszel.)

**Fig 2.** Survival forest plots. (A) Global survival: hazard ratio (HR), 0.86 (95% CI, 0.66–1.13; \( p = 0.28 \)). (B) Survival in which only studies with propensity-matched controls were included: HR, 1.05 (95% CI, 0.92–1.19; \( p = 0.51 \)). (CI = confidence interval; IV = inverse variance; SE = standard error.)
probable explanation for heterogeneity, with a coefficient B of 0.637 ($p = 0.035$) (Table 3; Fig 3A). When outliers were removed [13], surgical era as covariate gained much more strength in meta-regression analysis ($B = 0.97; p < 0.001$) (Fig 3B).

LVEF, LV End Diastolic Diameter, and NYHA Classification

Follow-up echocardiograms and NYHA assessments were done after a mean of 50 [21], 36 [20], and 6 [19] months after operation. Pooled analysis revealed a mean difference in LVEF of 0.48% (95% CI, −3.25 to 4.22%; $p = 0.8$). Although Chan and colleagues [23] did not report mean LVEF before and after operation, they described similar improvement in LV function between both groups at follow-up. No differences in LV end diastolic diameter (−0.09; 95% CI, −0.35 to −0.16; $p = 0.47$) and NYHA change (0.01; 95% CI, −0.60 to 0.61; $p = 0.98$) were found (Fig 4).

Reoperation

Reoperation because of endocarditis or recurrent MR (caused by paravalvular leak or failed repair) was reported in 4 studies [11, 19, 20, 24]. The OR was 1.49 (95% CI, 0.91−2.46; $p = 0.16$) (Fig 5A).

Recurrence of MR

Information was gathered regarding recurrence of MR $2+$ or greater on follow-up. Studies concluded that MVP results in an increase in recurrence of MR during the follow-up. The pooled OR was 7.51 (95% CI, 3.7−15.23; $p < 0.001$) (Fig 5B).

Freedom From Valve-Related Morbidity and Mortality

Only 2 articles reported data regarding valve-related morbidity and mortality. Because of the small number of patients included, we decided to exclude this measurement.

Comment

The superiority of MVP has been established for patients with degenerative MR [6]. The advantages of MVP include lower operative mortality, better preservation of ventricular function, fewer valve-related complications—including thromboembolism, endocarditis, and anticoagulation-related bleeding events—and improved long-term survival [25−28]. The main disadvantage of MVP is recurrence of MR, which affects survival mainly in patients with MR $2+$ or greater [29]. The incidence of $2+$ or greater MR varies from 11% [30] at 16 months to 72% [31] at 60 months. Predictors of recurrence at follow-up have been described [3, 22, 32].

Although the main advantage of MVR is the low incidence of recurrence of MR, its Achilles heel is the increased thromboembolic risk compared with MVP [33].

 Debate exists about the benefit of MVR or MVP regarding hospital mortality, survival, ventricular remodeling, and changes in LVEF, among other functional indicators in patients with IMR. Previous meta-analyses [12, 34] confirmed that MVR is associated with increased hospital mortality and lower survival.

We have included a total of 12 studies that address the outcomes of MVP versus MVR for IMR. These studies were selected after rigorous inclusion and exclusion criteria, aiming to reflect current surgical practice. The advantages of ring annuloplasty over suture or bovine pericardium annuloplasty have been established [35]. Even though a minority of specialized surgical centers obtain excellent short- and long-term results with suture annuloplasty [36, 37], we excluded articles in which more than 20% of procedures lacked an annuloplasty ring. Because of the evident short- and long-term benefit of preservation of the subvalvular apparatus at MVR [27],

### Table 3. Meta-Regression Analysis for Predictors of Heterogeneity in Survival

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<tr>
<th>Predictor</th>
<th>B Coefficient</th>
<th>p Value</th>
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<tbody>
<tr>
<td>Surgical era</td>
<td>0.637</td>
<td>0.035</td>
</tr>
<tr>
<td>Propensity-matched studies</td>
<td>0.041</td>
<td>0.95</td>
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Fig 3. Regression analysis for survival and surgical era. (A) Global analysis. (B) Excluding outliers (Cohn et al [10]).
we excluded articles in which there was no preservation in more than 20% of cases.

**Mortality**

Our results suggest that MVP is associated with lower in-hospital mortality, with a pooled OR similar to that in other individual studies [12, 34]. When we included only studies in which the majority of patients were operated on after 1998, no difference between MVP and MVR were found. Assuming a similar patient risk profile before and after 1998, hospital mortality is mainly related to surgical technique (subvalvular preservation), myocardial preservation (cardioplegia), extracorporeal circulation, and postoperative management. A number of changes have been introduced over time in all of these areas, which could explain the decrease in hospital mortality in MVR after 1998.

**Survival**

There was no difference in long-term survival. This meta-analysis reports similar long-term survival between MVP and MVR for IMR. Probable explanations for our results compared with those of Vassileva and coworkers [12] and Rao and colleagues [34], which reported a survival advantage of MVP, are the following: (1) Both studies included results from Al-Radi and associates [38], who reported the lack of preservation of the subvalvular apparatus in more than 20% of cases. Al-Radi and associates confirmed a survival advantage of MVP over MVR at 1 year, whereas no differences were found in the long term. This difference in survival could probably be explained by the higher hospital mortality in patients with MVR (OR of 17.2 against MVR), which might be related to the lack of preservation of the subvalvular apparatus.

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**Fig 4.** Forest plots. (A) Change in left ventricular (LV) ejection function. (B) LV end diastolic dimensions. (C) New York Heart Association (NYHA) class forest plots. (CI = confidence interval; df = degrees of freedom; IV = inverse variance; SD = standard deviation; Std. = standard.)

**Fig 5.** Forest plots. (A) Mitral regurgitation recurrence 2+ or greater. (B) Reoperation forest plots. (CI = confidence interval; df = degrees of freedom; M-H = Mantel-Haenszel.)
apparatus. (2) Vassileva and colleagues [12] did not include results from Cohn and colleagues [10], which favored MVR over MVP, in their analysis. (3) Rao and associates [34] included the study from Gillinov and coworkers [39], who performed a subgroup analysis of survival according to preoperative risk. There is no information in their report regarding global survival or mortality. Therefore, this contribution was not included in the analysis. (4) These meta-analyses did not include the contributions of Chan and coworkers [23], Lorusso and associates [11], Maltais and colleagues [17] and Qiu and colleagues [21], reporting no survival difference between treatments.

Functional Factors and Recurrence of MR
Both techniques provide similar benefit in cardiac remodeling, EF improvement, and NYHA class. Although the incidence of reoperation was similar in both treatment modalities, MVP increased the odds of recurrence of MR (≥2+) 7 times. This latter finding is extremely important. As mentioned earlier, recurrence of MR 2+ or greater has an impact on survival [29]. Similar reoperation rates between both groups suggest that surgeons who perform MVP establish a high threshold for reintervention in these patients.

Limitations
This meta-analysis includes observational studies with the inherent bias of retrospective reviews, among them the recent study of Lorusso and associates [14], which represents a substantial proportion of the total number of patients included in the analysis and could therefore dominate the results. Few studies compared changes in LVEF, LV diastolic dysfunction, and NYHA class, which weakened the conclusions. Inspection of funnel plots revealed fairly symmetrical distributions and did not raise any major concerns about the potential of publication bias. However, the possibility of such bias still exists and should be taken into account when considering the results.

The lack of patient selection in the studies based on predictive factors of recurrence of MR, as well as low performance of adjunctive repair techniques, could negatively affect the long-term results of MVP reported in our study.

Conclusions
Hospital mortality is lower in patients treated with MVP compared with those treated with MVR. MR recurrence is higher with MVP. There is no difference in long-term survival between the 2 groups. Recurrence of MR and thromboembolic risk are the main factors regarding survival in MVP and MVR, respectively. Therefore, the choice of MVP or MVR should be individualized in each patient, taking into account predictors of recurrence and thromboembolic risk.

References
INVITED COMMENTARY

The appropriate approach to functional ischemic mitral regurgitation (IMR) continues to evolve. At issue is whether or not it should be addressed surgically and, if so, the best surgical approach. Mitral valve repair (MVP) is clearly superior for degenerative disease because of the low failure rates and the preservation of ventricular geometry. In the setting of ischemic disease, the advantage of MVP is less clear because of the significant recurrence rates within 6 months of operation [1].

Most IMR has two causes: annular dilatation (type I) and leaflet retraction (type IIIb). The technique most frequently used in MVP for IMR is simple reduction annuloplasty, which does not address leaflet restriction and may not prevent further ventricular remodeling. Techniques to address these issues include anterior leaflet augmentation, transection of second-order chords, and posterior papillary muscle relocation. All attempts to improve leaflet coaptation to compensate for further remodeling [2, 3]. These techniques improve the results in small series, although long-term data are limited, and the techniques have not been widely disseminated.

This raises a general question: is MVP better than mitral valve replacement (MVR) in the setting of IMR? No randomized trials have evaluated this question.

Dayan and colleagues [4] try to address this question through a meta-analysis. An extensive literature review subject to strict inclusion criteria showed that although early failures are more common after MVP, long-term survival is similar after MVP and MVR. In the current era, operative mortality has decreased and is similar in both approaches.

These data suggest that surgeons should critically reevaluate the approach to patients undergoing valve operations for IMR. Chordal-sparing MVR may better serve patients with substantial distortion of mitral valve apparatus, severe ventricular dilation, and residual leak after MVP or those in whom significant ventricular remodeling may be anticipated.

Although the benefits of MVP over MVR have been extensively demonstrated in nonischemic mitral...