Mitral Repair versus Replacement for Ischemic Mitral Regurgitation

Comparison of Short-Term and Long-Term Survival

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Background—When compared to mitral valve replacement (MVR), mitral valve repair (MVRp) is associated with better survival in patients with organic mitral regurgitation (MR). However, there is an important controversy about the type of surgical treatment that should be used in patients with ischemic MR. The objective of this study was to compare the postoperative outcome of MVRp versus MVR in patients with ischemic MR.

Methods and Results—Preoperative and operative data of 370 patients with ischemic MR who underwent mitral valve surgery were prospectively collected and retrospectively analyzed. MVRp was performed in 50% of patients (n=186) and MVR in 50% (n=184). Although operative mortality was significantly lower after MVRp compared to MVR (9.7% versus 17.4%; P=0.03), overall 6-year survival was not statistically different between procedures (73±4% versus 67±4%; P=0.17). After adjusting for other risk factors and propensity score, the type of procedure (MVRp versus MVR) did not come out as an independent predictor of either operative (OR, 1.5; 95% CI, 0.7–2.9; P=0.34) or overall mortality (HR, 1.2; 95% CI, 0.7–1.9; P=0.52).

Conclusion—As opposed to what has been reported in patients with organic MR, the results of this study suggest that MVRp is not superior to MVR with regard to operative and overall mortality in patients with ischemic MR. These findings provide support for the realization of a randomized trial comparing these 2 treatment modalities. (Circulation. 2009;120[suppl 1]:S104–S111.)

Key Words: ischemia ■ mitral valve ■ prosthesis ■ regurgitation ■ valves

Ischemic mitral regurgitation (MR) is a complication of coronary artery disease that is associated with poor outcomes.1,2 The basic mechanism of ischemic MR is the remodeling of the ischemic left ventricle (LV), which, in turn, may lead to displacement of the papillary muscles, annular dilatation, and leaflet tethering. Although there is robust evidence that mitral valve repair (MVRp) is superior to mitral valve replacement (MVR) for the correction of organic MR, there is still an important dilemma as to which procedure is the most appropriate for management of ischemic MR.3,4 Restrictive mitral valve annuloplasty is currently the most frequently used technique for the surgical management of patients with severe ischemic MR.5 However, this procedure is associated with 10% to 20% rates of persistent MR early after operation and with 50% to 70% rates of recurrent MR at 5 years.5 Furthermore, the presence of persistent or recurrent MR is associated with higher incidence of cardiac events6 and reduced survival.6 The objective of this study thus was to compare MVRp and MVR with respect to operative and overall mortality in patients with chronic ischemic MR.

Materials and Methods

We retrospectively reviewed the preoperative, operative, and post-operative data of 370 patients with chronic ischemic MR who underwent mitral valve surgery with or without coronary artery bypass graft surgery between January 1995 and January 2008 at Laval Hospital/Québec Heart & Lung Institute. Exclusion criteria were: (1) acute ischemic MR; (2) nonischemic dilated cardiomyopathy; (3) concomitant organic MR; (4) aortic or pulmonary valve stenosis or regurgitation more than mild; (5) severe tricuspid regurgitation; (6) previous mitral valve surgery; and (7) concomitant surgery on another valve than mitral.

We retrospectively reviewed the data that were prospectively collected in a computerized database. Baseline preoperative and operative variables were defined according to the guidelines of the Society of Thoracic Surgeons. Preoperative heart failure was defined as the occurrence of acute pulmonary edema, paroxysmal nocturnal dyspnea, or pulmonary congestion documented by chest X-ray in the 2 weeks preceding surgery. LV ejection fraction was assessed before surgery using either echocardiographic or angiographic methods in 97% of the patients. Echocardiographic measures of LV end-diastolic and end-systolic dimensions were available in 69% of patients. Patients were categorized as having ischemia and classified as mild (grade I), moderate (grade II), or severe (grades III and IV).7 All patients had a type IIIb MR etiology.
Preoperative and operative variables were compared between the 2 treatment groups using \( t \) test, \( \chi^2 \) test, or Fisher exact test as appropriate. Postoperative MR severity was compared between groups with \( \chi^2 \) test. Cumulative survival was estimated with the Kaplan-Meier method and compared between groups using a log-rank test. Univariate and multivariate analyses were performed to determine whether the type of surgical procedure (ie, MVRp versus MVR) was significantly associated with survival after adjustment for potential confounders. Clinically relevant variables with \( P < 0.1 \) on univariate analysis were incorporated into the multivariate models. Stepwise logistic regression and Cox proportional-hazards regression analyses were performed to identify independent predictors of operative and overall mortality, respectively. Proportionality of the hazard was visually inspected from log-minus-log survival curves, stratified by the variable of interest and adjusted for the other variables. Hazard proportionality was also assessed by testing the interaction between variables of interest and time in an adjusted model. If the hazard ratio (HR) of a variable changed significantly over time, the variable was replaced by 2 new time-dependent covariates in the Cox regression model.

To eliminate covariate differences that may lead to biased estimates of treatment effect, a propensity score adjustment was also used. A propensity score representing the probability of having MVR as opposed to MVRp was calculated for each patient by using a logistic regression analysis that identified variables independently associated with the type of surgical procedure. The calculated propensity score was then incorporated into subsequent multivariate models. In addition, 2 groups of 104 patients receiving either MVRp or MVR were matched on a 1:1 basis according to propensity score using nearest neighbor method with a caliper of 0.01. As appropriate, the impact of the type of surgery on operative and overall mortality was obtained using McNemar’s test and stratified univariate Cox model, respectively.

## Statistics

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## Results

Among the 370 patients included in this study, 186 received MVRp (50%) and 184 (50%) received MVR. Table 1 shows preoperative variables in these 2 groups. Compared to patients with MVRp, those with MVR had higher Parsonnet score prevalence of preoperative renal failure, heart failure, pulmonary hypertension, New York Heart Association functional class more than III, and severe MR (Table 1). They also had a lower proportion of concomitant CABG. After
Operative mortality was significantly (P=0.03) lower (7.5%) in the MVRp group than in the MVR group (16%). However, after adjusting for other risk factors and propensity score, the type of surgical procedure was no longer a significant predictor of operative mortality (OR, 1.3; CI, 0.3–1.7; P=0.32).

### Overall Mortality

The mean follow-up in this series was 3.8±3.9 years (25% quartile, 0.6; median, 2.6; 75% quartile, 5.3). During follow-up, 96 patients died and the overall survival was 69±3% at 6 years and 48±6% at 12 years. Death was of cardiovascular cause in 62 patients and 6-year and 12-year freedom from cardiovascular-related death was 79±3% and 66±9%, respectively. Survival rate was similar (P=0.17) in patients who underwent MVR (6-year, 67±4%; 12-year, 47±7%) compared to those who underwent MVRp (6-year, 73±4%; 12-year, 48±13%; Figure 1A). There was also no significant difference between the 2 groups with regard to freedom from cardiovascular death (MVR 6-year, 76±4%; 12-year, 67±6%; MVRp 6-year, 84±3%; 12-year, 55±14%; Figure 1B).

On univariate analysis, the predictors of overall mortality were age, renal failure, recent heart failure, advanced New York Heart Association functional class, and the measured intertrigonal length. The operative mortality was significantly (P=0.03) lower (7.5%) in the MVRp group than in the MVR group (16%). However, after adjusting for other risk factors and propensity score, the type of surgical procedure was no longer a significant predictor of operative mortality (OR, 1.3; CI, 0.3–1.7; P=0.32).

### Table 2. Operative Data

<table>
<thead>
<tr>
<th>Variables</th>
<th>All Patients (n=370)</th>
<th>MV Repair (n=186; 50%)</th>
<th>MV Replacement (n=184; 50%)</th>
<th>P</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urgent status, n (%)</td>
<td>155 (42)</td>
<td>67 (36)</td>
<td>88 (48)</td>
<td>0.03</td>
<td>NS</td>
</tr>
<tr>
<td>CPB time, min</td>
<td>135±42</td>
<td>134±42</td>
<td>137±42</td>
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<td>NS</td>
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<tr>
<td>ACC time, min</td>
<td>99±30</td>
<td>100±29</td>
<td>99±32</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Concomitant CABG, n (%)</td>
<td>328 (89)</td>
<td>174 (94)</td>
<td>154 (84)</td>
<td>0.002</td>
<td>NS</td>
</tr>
<tr>
<td>Ring type, n (%)</td>
<td></td>
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<td>Carpenter Edwards</td>
<td>...</td>
<td>145 (78)</td>
<td>...</td>
<td></td>
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</tr>
<tr>
<td>CMA IMR Eltlogix</td>
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<td>35 (19)</td>
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<tr>
<td>Duran</td>
<td>...</td>
<td>6 (3)</td>
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<td>Prosthesis type</td>
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<td>Mechanical, n (%)</td>
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<td>...</td>
<td>145 (79)</td>
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<td>St. Jude Mechanical</td>
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<td>...</td>
<td>70 (38)</td>
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<td>Bioprosthesis, n (%)</td>
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<td>...</td>
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<td>Ring/prosthesis size, n (%)</td>
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<td>24 mm</td>
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<td>26 mm</td>
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<td>30 mm</td>
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<td>21 (11)</td>
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<tr>
<td>31–33 mm</td>
<td>...</td>
<td>15 (8)</td>
<td>6 (3)</td>
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</tbody>
</table>

ACC indicates aortic cross-clamp; CABG, coronary artery bypass graft; CMA, Carpentier-McCarthy-Adams; CPB, cardiopulmonary bypass.

*P after adjustment for propensity score.

adjutment for propensity score, all the differences between MVRp and MVR groups became nonsignificant (Tables 1, 2).
York Heart Association functional class (ie, NYHA III), and reduced LV ejection fraction (Table 4). Univariate predictors of cardiovascular mortality were age, male gender, chronic lung disease, renal failure, heart failure, and reduced LV ejection fraction. However, the type of procedure (ie, MVRp versus MVR) was not a significant predictor of overall or cardiovascular mortality.

On multivariate analysis, age, male gender, recent heart failure, and reduced LV ejection fraction were independently associated with overall mortality (Table 4). Multivariate predictors of cardiovascular mortality were age, male gender, chronic lung disease, renal failure, heart failure, and reduced LV ejection fraction. The type of procedure was not a significant predictor of overall or cardiovascular mortality.

There was a change in overall mortality HR of MVRp versus MVR over time. We therefore replaced into the model the MVRp versus MVR variable by 2 time-dependent covariates: one for the early hazard phase and a second one for the late hazard phase. According to the visual inspection of log-minus-log survival curves, the most appropriate time cut-off value to separate these 2 phases was 6 months. On univariate analysis, the type of procedure (ie, MVRp versus MVR) had no impact on survival after 6 months ($P=0.71$), whereas it had a significant impact before 6 months ($P=0.035$). On multivariate analysis, the type of procedure resulted in similar survival after 6 months (HR for MVRp versus MVR=1.1; 95% CI, 0.5–2.1; $P=0.84$) but showed a trend for an impact on early mortality (HR for MVRp versus MVR, 0.6; 95% CI, 0.3–1.1; $P=0.10$). When adjusting for propensity score, the effect of the type of procedure on <6 months survival was not significant (HR, 0.7; 95% CI, 0.4–1.2; $P=0.19$).

**Propensity Score-Matched Cohorts**

There was no significant difference between the 2 propensity score-matched groups (n=104 in both groups) with regard to preoperative and operative data. Operative mortality was not significantly ($P=0.26$) different in MVRp (10%) versus MVR (15%) patients. Overall survival (Figure 2) of patients who underwent MVRp was similar ($P=0.48$) to those of patients with MVR (4-year, 76±5% versus 76±5%; 8-year, 65±7% versus 68±7%, respectively).

**Incidence of Persistent MR According to the Type of Procedure**

At predischarge echocardiographic examination, the prevalence of persistent MR was significantly higher in the MVRp group than in the MVR group (Figure 3).

**Discussion**

The main finding of this study is that as opposed to what has been reported in patients with organic MR, there is no evidence that MVRp provides better short-term or long-term survival compared to MVR in patients with ischemic MR. MVRp was associated with reduced operative mortality on univariate analysis but this association was no longer significant after adjustment for preoperative risk factors and propensity score or propensity score matching. Moreover, there was no difference between the 2 procedures with regard to long-term survival.

In patients with organic MR, MVRp is associated with better survival compared to MVR, even after adjusting for
differences in baseline characteristics. The difference in survival between MVRp and MVR in this population appears to be more important in the early postoperative period, whereas the survival curves tend to become parallel in the longer-term. The outcome of patients undergoing MVR may be affected by prosthetic valve thrombogenicity, durability, and hemodynamics. Thromboembolic complications are an important cause of morbidity and mortality in patients with a prosthetic valve. The risk of thromboembolic events is higher with mitral than with aortic prosthetic valves, with mechanical than with bioprosthetic valves, and in the early (<3 months) versus late postoperative phases. Moreover, the rate of structural valve deterioration in bioprosthetic valves increases over time, particularly after the initial 8 to 10 years after implantation, and thereby exposes the patient to the risk of reoperation. Risk factors previously found to be associated with accelerated structural valve deterioration include younger age and mitral valve position. Finally, severe prosthesis–patient mismatch after MVR has been associated with reduced postoperative survival.

In 1995, Bolling et al introduced the concept of performing undersized (or restrictive) annuloplasty for the treatment of ischemic MR by implanting rings 1 or 2 sizes smaller than the measured intertrigonal length. Despite the fact that ischemic MR is in essence “a ventricular and not a valvular disease” and that restrictive mitral annuloplasty targets the consequence (ie, MR) rather than the cause of the disease, some studies reported relatively good results in terms of MR correction and improvement of outcomes. However, other studies have reported significant rates of persistent or recurrent MR after this procedure. The mechanism underlying the persistence of MR after MVRp in ischemic MR patients is likely related to the persistence or worsening of the tethering of mitral valve leaflets, especially the posterior leaflet. However, the mechanism of recurrent MR is related to progressive continued LV negative remodeling, which increases LV dimension and sphericity, and thus valve tethering. Postoperative persistence or recurrence of MR, even if only mild, should not be viewed as a benign complication. Residual MR contributes to negative LV remodeling, which may in turn generate a vicious circle in which MR begets more MR. To this effect, 2 recent studies demonstrated that the presence of persistent or recurrent MR is associated with markedly worse outcomes.

Hence, MVRp may avoid the aforementioned complications related to prosthetic valve implantation, however, this may be counterbalanced by the relatively high rates of persistent/recurrent MR associated with MVRp in this population with ischemic MR. Moreover, we recently demonstrated that restrictive annuloplasty may also induce functional mitral stenosis that may, in turn, negatively impact postoperative outcomes. Hence, both persistent/recurrent MR and iatrogenic mitral stenosis may contribute to the lack of benefit of MVRp over MVR in patients with ischemic MR.

Some studies reported that unadjusted survival is lower with MVR than with MVRp in patients with ischemic MR. However, as also observed in the present study (Table 1), patients undergoing MVR are frequently older, sicker, and have more comorbidities than those with MVRp, which may explain survival differences between the 2 treatment groups. To this effect, Cohn et al demonstrated that the outcome of patients with ischemic MR is more related to the patient’s clinical status rather than to the type of procedure (MVR versus MVRp). Consistently, Grossi et al reported that the type of procedure has little influence on prognosis after adjustment for preoperative New York Heart Association class. Moreover, in their study, MVR provided better and more durable correction of MR in the subset of patients with severe ventricular-papillary dysfunction. Enríquez-Sarano et al also reported that although MVRp is associated with a better survival rate than that seen after MVR in organic MR, there is no clear benefit from MVRp in ischemic MR. Using propensity score-matched cohorts, Gillinov et al found that MVRp provides better postoperative outcomes compared to MVR. However, in high-risk patients, survival was similar with both types of procedure. In the present study, we found no significant difference between MVRp and MVR with regard to short-term and long-term survival in patients with ischemic MR after adjusting or matching for propensity score.
The baseline LV ejection fraction in the present series is higher than that reported in some previous studies, but similar to that found in other studies. These discrepancies underline the point that ischemic MR is a complex and highly heterogeneous entity that is, in large part, determined by the development of global or local adverse LV remodeling, which, in turn, results from the extent and localization of the myocardial infarction. Hence, although ischemic MR is often associated with reduced LV ejection fraction, a large proportion of patients with chronic ischemic MR have no or mild global LV systolic dysfunction. Even a local LV remodeling with limited alteration of the global LV geometry and function is sufficient to cause a severe ischemic MR and negatively impact patient outcome before and after surgery.

The findings of the present and previous studies underline the importance of tailoring the surgical procedure according to the baseline characteristics of the patient. Several studies have indeed demonstrated that it is possible to predict the risk of persistent MR and, to a lesser extent, the risk of recurrent MR after MVRp from the preoperative echocardiographic evaluation. The factors that were identified as independent predictors of MVRp failure in patients with ischemic MR were large LV end-diastolic diameter, mitral annulus diameter, mitral valve tenting area, coaptation distance, and posterior leaflet angle. MVR or alternative procedures targeting the mitral valve apparatus or the LV should be contemplated in the patients identified as

**Clinical Implications**

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<table>
<thead>
<tr>
<th>Variables</th>
<th>Preoperative</th>
<th>Operative</th>
<th>Propensity score</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Preoperative</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, yr</td>
<td>&lt;0.001</td>
<td>0.17</td>
<td>0.008</td>
</tr>
<tr>
<td>Male</td>
<td>0.051</td>
<td>0.14</td>
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</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>0.75</td>
<td>0.07</td>
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<tr>
<td>Hypertension</td>
<td>0.74</td>
<td>0.13</td>
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<tr>
<td>Diabetes</td>
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<tr>
<td>Chronic lung disease</td>
<td>0.06</td>
<td>0.16</td>
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<tr>
<td>Renal failure</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
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<tr>
<td>Atrial fibrillation</td>
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<td>0.07</td>
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<tr>
<td>Pulmonary hypertension</td>
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<tr>
<td>Stroke</td>
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<td>0.14</td>
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<tr>
<td>Recent heart failure</td>
<td>&lt;0.001</td>
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<td>NYHA functional class III</td>
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<tr>
<td>LV ejection fraction, per %</td>
<td>0.015</td>
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</tr>
<tr>
<td>Severe mitral regurgitation</td>
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<td>0.17</td>
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<tr>
<td>MVRp versus MVR</td>
<td>0.17</td>
<td>0.17</td>
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</tr>
</tbody>
</table>

**Table 4. Univariate and Multivariate Predictors of Overall Mortality**
being at high risk for MVRp failure based on preoperative echocardiography.

The findings of the present study give support for the realization of a randomized trial comparing MVRp versus MVR for the treatment of chronic ischemic MR. To this effect, there is an ongoing NIH-funded clinical trial to assess the safety and efficacy of MVRp versus MVR for patients with severe ischemic MR. The results of the present study also provide an impetus to develop new surgical procedures to enhance early and late outcomes of ischemic mitral valve repair.

**Study Limitations**

This is a single-institution, nonrandomized, retrospective study. We attempted to compensate for the lack of randomization by propensity score matching. However, one cannot take into account all the potential bias related to the selection of the operative therapy in this complex disease. Nonetheless, the unadjusted overall survival was comparable among the 2 treatment groups even though the risk profile favored the MVRp group.

The 13-year span of our series encompassed changing surgical techniques. In particular, restrictive ring annuloplasty for the treatment of ischemic MR has been introduced in the late 1990s. Hence, in the first years of this series, undersized annuloplasty was not performed in a systematic and standardized manner in all patients. Nonetheless, a subanalysis in the subset of patients who underwent operation after 2000 showed a reduced operative mortality compared to the previous period but similar results between the 2 operative strategies.

The results of MVRp and MVR were evaluated intraoperatively by transesophageal echocardiography. However, previous studies have demonstrated that intraoperative echocardiography may substantially underestimate the presence and severity of residual ischemic MR after MVRp. Anaesthesia may change preload and afterload conditions, and therefore LV dimensions and degree of leaflet tethering. Although no patient left the operating room with more than mild MR in this series, a moderate MR (ie, grade II) was observed in 18% of the patients at predischarge examination, and this incidence is similar to what has been reported in other studies.

The follow-up echocardiographic data after discharge were not available in a large proportion of the patients included in this study. Hence, we did not have the complete data on the incidence of late MR recurrence and on the evolution of LV ejection fraction and LV dimensions after operation. Thus we were not able to assess the impact of MR recurrence on postoperative survival. However, recent studies that specifically examined this issue have reported that recurrent MR after MVRp for ischemic MR is associated with worse outcomes.

**Conclusion**

As opposed to what has been reported in patients with organic MR, we found no evidence that MVRp provides any benefit in terms of short-term or long-term survival compared to MVR in patients with ischemic MR. These findings emphasize the need of a randomized prospective trial comparing these 2 operative strategies and provide an impetus for the development of new surgical techniques that directly target the causal mechanisms of this complex disease.

**Acknowledgments**

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**Disclosures**

Drs Pibarot, Mathieu, Dumesnil, Charbonneau, Dagenais, and Voisine hold consultancies and/or are on the speaker’s bureau of Edwards Life Sciences, Medtronic, St. Jude Medical, and Sorin. They also have received research grants or products (prosthetic valves for in vitro or animal experimental studies) from these companies.

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