Preoperative Posterior Leaflet Angle Accurately Predicts Outcome After Restrictive Mitral Valve Annuloplasty for Ischemic Mitral Regurgitation

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Background—Ischemic mitral regurgitation (MR) often persists after restrictive mitral valve annuloplasty, in which case it is associated with worse clinical outcomes. The goal of the present study was to determine whether persistence of MR and/or clinical outcome could be predicted from preoperative analysis of mitral valve configuration.

Methods and Results—In 51 consecutive patients undergoing restrictive annuloplasty for ischemic MR, posterior leaflet (PL) angle, anterior leaflet angle, coaptation distance, and tenting area were quantified by echocardiography before surgery (6±3 days), and MR severity was assessed before and early after surgery (9±4 days). Postoperatively, persistence of mild to moderate MR (vena contracta ≥3 mm) was observed in 11 (22%) of the patients. The best predictor of postoperative persistence of MR was a PL angle ≥45 degrees (sensitivity 100%, specificity 97%, positive predictive value 92%, negative predictive value 100%). Patients with persistent MR had markedly lower 3-year event-free survival (26±20% compared with those with nonpersistent MR (75±12%, P=0.01). Preoperative presence of a PL angle ≥45 degrees also was associated with a markedly lower 3-year event-free survival (22±17% versus 76±12%; P<0.001).

Conclusions—In patients undergoing restrictive annuloplasty for ischemic MR, persistence of MR and 3-year event-free survival can accurately be predicted by preoperative analysis of mitral valve configuration. Patients with a PL angle ≥45 degrees (ie, with high PL restriction) should thus be considered poor candidates for this procedure, and concomitant or alternative procedures should be contemplated. (Circulation. 2007;115:782-791.)

Key Words: mitral valve ■ echocardiography ■ ischemia ■ regurgitation

Ischemic mitral regurgitation (MR) is a serious complication of coronary artery disease and is associated with poor outcomes.1,2 The basic mechanism of ischemic MR is remodeling of the ischemic left ventricle (LV), leading to displacement of the papillary muscles, annular dilatation, and leaflet tethering. These modifications of the LV and mitral valve geometry prevent normal leaflet coaptation.3 Restrictive mitral valve annuloplasty (MVA) combined with coronary artery bypass graft (CABG) is the conventional approach for the surgical management of patients with ischemic MR.4 Recent studies have failed to demonstrate a significant impact of this procedure on long-term survival, however.5-7 This finding may be attributable, at least in part, to the persistence or recurrence of MR in these patients. Indeed, previous studies have demonstrated that MR often persists or recurs after MVA8-10 and can adversely affect a patient’s outcome.11 In a recent study by Zhu et al,10 persistent MR was present in 19% of patients early after operation. The persistence of MR after MVA could be explained by the postoperative persistence of tethering of both leaflets and/or by worsening of posterior leaflet (PL) tethering that is potentially caused by ring prosthesis implantation, which may anteriorly displace the PL and reduce its mobility.10,12-14 McGee et al9 report that 28% of patients have 3+ or 4+ MR and that 25% have 2+ MR 6 months after MVA. Among these patients with ≥2+ MR at 6 months, approximately 40% already had significant persistent MR early after operation.

Clinical Perspective p 791

The objective of the present study was to determine whether the preoperative echocardiographic indices of mitral valve configuration could be used to accurately predict the persistence of MR and outcomes after MVA in patients with ischemic MR.

Methods

Study Population

The echocardiograms of 70 consecutive patients with ischemic MR who underwent surgery for restrictive MVA with or without CABG at the Quebec Heart Institute between January 2002 and December
2005 were analyzed for the present study. Patients were excluded from the study if they had concomitant organic mitral valve lesions, significant aortic regurgitation, or significant aortic stenosis. The final study group was composed of 51 patients (42 men, 9 women; mean age, 65 ± 8 years). Moreover, 20 healthy subjects with no history of cardiovascular disease and with normal Doppler echocardiographic examination were recruited for the control group. These control subjects had a gender distribution and average body size similar to those of the patients with ischemic MR.

**Surgical Technique**

The mitral valve was assessed intraoperatively through a standard left atriotomy. A complete ring annuloplasty was performed in the majority (88%) of patients using a Physio ring (Edwards Lifescience, Irvine, Calif). Ring size was selected by downsizing the measured intertrigonal length by 2 sizes. Intraoperatively, the MVA was evaluated by transesophageal echocardiography. In presence of MR, either a smaller-size annuloplasty or a mitral valve replacement was performed. In these cases, the patients were excluded from the retrospective series. Moreover, every vessel that could be grafted was grafted.

**Echocardiographic Measurements**

Two-dimensional and Doppler transthoracic echocardiography examinations with commercially available echocardiographic systems (Sonos 5500 or 7500, Philips Medical Systems, Amsterdam, the Netherlands) were performed 6 ± 3 days (range, 1 to 19 days) before surgery and 9 ± 4 days (range, 1 to 15 days) after surgery at the time of predischarge examination.

**LV Geometry and Function**

The LV end-diastolic and end-systolic diameters were measured using M-mode in the parasternal long-axis view. LV end-diastolic and end-systolic volumes and LV ejection fraction were determined by the modified biplane Simpson method. To assess the LV shape, LV end-diastolic and end-systolic sphericity indices were calculated by dividing the LV short-axis dimension by the LV long-axis dimension in the 4-chamber view. The LV outflow tract stroke volume was calculated by multiplying the LV outflow tract area by the LV outflow tract velocity-time integral measured by pulsed-wave Doppler. The closing forces index was evaluated by multiplying the systolic blood pressure by the mitral annulus area.

**Figure 1. Method of mitral leaflet angle quantification. A, Schema of transthoracic echocardiographic 4-chamber view in midsystole. B, Echocardiographic image demonstrating technique of measurements of anterior leaflet angle (ALA) and posterior leaflet angle (PLA) using coaptation distance (CD), bending distance (BD), anterior leaflet bending distance (ALBD), and posterior leaflet length (PLL). RA indicates right atrial; RV, right ventricle.**

**Mitral Valve Configuration and Left Atrial Geometry**

Mitral valve configuration was assessed in midsystole using the parasternal long-axis and 4-chamber views (Figure 1). The mitral valve tenting area was measured as the area enclosed between the annular line and mitral valve leaflets. The coaptation distance was defined as the distance between the annular line and the leaflet’s coaptation point. The PL angle and the anterior leaflet angle were calculated according to the following formulas:

\[
\text{PLA} = \sin^{-1}\left(\frac{\text{CD}}{\text{PLL}}\right)
\]

\[
\text{ALA} = \sin^{-1}\left(\frac{\text{BD}}{\text{ALBD}}\right)
\]

where PLA is the PL angle, CD is the coaptation distance, and PLL is the PL length (ie, the distance between the posterior annulus and the PL tip). In the second formula, ALA is the anterior leaflet angle, BD is the bending distance (ie, the distance between the anterior leaflet bending and annular line), and ALBD is the anterior leaflet bending distance (ie, the distance between anterior annulus and anterior leaflet bending point).

Left atrial (LA) geometry was assessed by LA diameter measured in the parasternal long-axis view using M-mode and LA area measured in 4-chamber view with the use of 2-dimensional planimetry.

**MR Assessment**

MR was assessed quantitatively using the width of the vena contracta of the regurgitant jet and the ratio of the MR color flow jet area to the LA area. Vena contracta width was measured in the parasternal long-axis view. The largest diameter during systole was measured in at least 3 cardiac cycles and was then averaged.
Postoperative Outcome

Postoperative cardiac events were defined as rehospitalization for congestive heart failure, mitral valve replacement or repair, heart transplant, or cardiovascular-related death.

Prospective Series

We prospectively analyzed the preoperative and early postoperative echocardiograms (5 ± 2 days after surgery) of 21 consecutive patients with ischemic MR between January 2006 and October 2006. These patients were referred for CABG and MR correction. Among these 21 patients, 4 were excluded because of the presence of concomitant organic lesions. The final prospective subset was composed of 17 patients (11 men, 6 women; 64 ± 8 years).

Statistical Analysis

Interobserver and intraobserver variability for measurement of vena contracta width and mitral valve configuration parameters was determined from the analysis of the Doppler echocardiographic images of 14 randomly selected patients by 2 independent observers. The results were compared with a 1-way analysis of variance, Pearson correlation coefficient, and Bland-Altman method.

The patients were separated into 2 groups depending on the presence or absence of mild to moderate MR after MVA, defined as an early postoperative vena contracta ≥3 mm. These patients with persistence or early recurrence of significant MR were classified as the persistent MR group. Residual MR with a vena contracta width ≤3 mm was considered not clinically significant and was classified as nonpersistent MR. Results are expressed as mean ± SD or as percentages unless otherwise specified. Before analysis, normality distribution was tested using the Kolmogorov-Smirnov test. Preoperative Doppler echocardiographic indices of mitral valve configuration were compared among the persistent MR, nonpersistent MR, and control groups, using a 1-way analysis of variance.
TABLE 2. Preoperative and Postoperative Echocardiographic Data

<table>
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<tr>
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<th>Control (n=20)</th>
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<th>Postoperative</th>
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<td>58±7*</td>
<td>56±7‡</td>
<td>63±4‡(†)</td>
<td>61±5‡(†)‡</td>
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<td>Vena contracta width, mm</td>
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<td>5.9±1.2</td>
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<td>39±13</td>
<td>2±1‡</td>
<td>40±16</td>
<td>16±10†‡</td>
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</table>

Values are mean±SD. LVED indicates LV end-diastolic; LVES, left ventricular end-systolic.

The symbols in parentheses indicate that the difference was no longer significant after correction for type I error (ie, corrected P<0.05). The correction was performed by multiplying the P value by the number of variables (13) included in this comparison.

*Significant difference (P<0.05) vs control group.
†Significant difference (P<0.05) vs nonpersistent MR group.
‡Significant difference (P<0.05) between preoperative and postoperative data.

Results

Patient Characteristics

Of the 51 patients, 11 (22%) had persistent MR (vena contracta >3 mm), 10 (20%) had nonclinically significant MR (vena contracta 3 mm), and 30 (58%) had no detectable MR after surgery. There was no significant difference between the nonpersistent MR group (40 patients, 78%) and the persistent MR group (11 patients, 22%) in term of preoperative demographic and clinical data (Table 1). Myocardial infarction site was inferior in 39 patients (76%) and anterior in 12 patients (24%). Distribution of the myocardial infarct site did not differ between the persistent and nonpersistent groups. There was no significant difference between the 2 groups regarding medication. Operative data as well as ring size and type also were similar in both groups (Table 1).

Reproducibility of Echocardiographic Measurements

There was an excellent correlation (r≥0.90) between intraobserver measurements and also between interobserver measurements for all preoperative and postoperative echocardiographic parameters. Intraobserver and interobserver relative differences were <5% for all parameters (range for intraobserver, 0.8% to 4.6%; interobserver, 0.7% to 4.8%). The Bland-Altman method showed excellent agreement between interobserver and intraobserver measurement in both low and high values of echocardiographic parameters.

Echocardiographic Measurements

There were significant differences between the control subjects and the ischemic MR patients regarding the Doppler echocardiographic parameters of LV geometry and function, LA geometry, and mitral valve configuration (Tables 2 and 3). These differences persisted after operation, except for LV end-diastolic volume and sphericity index in the nonpersistent MR group.
With no significant difference between the 2 groups regarding visual estimation of inferior wall motion before and early after operation. Before operation, there was no significant difference with respect to vena contracta width, vena contracta width indexed to body surface area, or MR area:LA area ratio. After correction for type I error, however, there was only a significant difference between preoperative and postoperative LV end-diastolic diameters and higher preoperative parameters that were the most accurate in predicting a postoperative vena contracta width >3 mm were PL angle, coaptation distance, and tenting area (area under the curve = 0.98, 0.87, and 0.90, respectively). LV end-diastolic and end-systolic diameters were less accurate for the prediction of persistent MR (area under the curve = 0.74 for both parameters).

The preoperative presence of a PL angle ≥ 45 degrees had the best performance for the prediction of persistent MR: sensitivity, 100%; specificity, 95%; positive predictive value, 85%; negative predictive value, 100% (Figure 3). Tenting area ≥ 2.5 cm² and coaptation distance ≥ 1 cm also had a high specificity (≥ 90%), but their sensitivity was lower (64% for both parameters). Among the 8 (16%) patients with a PL angle ≥ 45 degrees, a tenting area ≥ 2.5 cm², and a coaptation distance ≥ 1 cm, 7 had persistent MR at hospital discharge, whereas among the 36 (71%) patients with a PL angle < 45 degrees, a tenting area < 2.5 cm², and a coaptation distance < 1 cm, none had persistent MR.

Among the preoperative and operative factors, PL angle ($\Delta r^2=0.47$, $P<0.001$), coaptation distance ($\Delta r^2=0.08$, $P=0.003$), and prosthesis ring size ($\Delta r^2=0.05$, $P=0.02$) were independently associated with larger postoperative vena contracta width on multivariate analysis.

**Postoperative Outcome**

Patients with persistent MR had markedly lower 3-year cardiac event-free survival compared with those with nonper-
sistent MR (26±20% versus 75±12%; P=0.01). Patients with PL angle ≥45 degrees also had significantly lower 3-year event-free survival (22±17% versus 76±12%; P<0.001; Figure 4). The outcomes for patients with PL angle ≥45 degrees are presented in Table 4. A PL angle ≥45 degrees was associated with a 2.5-fold increase in the risk of cardiac event (hazard ratio, 2.5; 95% CI, 1.4 to 4.9; P=0.002). Moreover, after adjusting for age, gender, LV ejection fraction, LV end systolic diameter, and prosthesis ring size, PL angle ≥45 degrees was associated with a 2.4-fold increase in the risk of cardiac events (95% CI, 1.3 to 5.0; P=0.009).

Echocardiographic Data and Postoperative Outcome in the Prospective Series
Of the 17 patients studied prospectively, 14 had a preoperative PL angle <45 degrees and underwent MVA and CABG. None of these patients had persistent MR after operation. The 6-month event-free survival in these patients was 94%, which is similar to that observed in the retrospective series. Three (18%) patients had preoperative PL angle ≥45 degrees. One of these patients underwent MVA and CABG and had persistent MR (vena contracta width=0.41) at predischarge examination (Table 4). Although 2 other patients with excessive PL tethering were initially scheduled for MVA, the surgeon decided, on the basis of PL angle, to do a crossover to mitral valve replacement. In light of the compelling results of our present retrospective study, some surgeons of our institution started to modify their practice and now consider mitral valve replacement as an alternative option to annuloplasty when there is evidence of excessive PL tethering at the preoperative examination. Our 2 patients who underwent valve replacement had no persistent MR after operation. As opposed to the vast majority of patients with a PL angle ≥45 degrees who underwent MVA, these patients had no adverse events during follow-up.

Discussion
To our knowledge, the present study provides the first demonstration that adverse outcomes after MVA can largely be predicted from the configuration of the mitral valve on the preoperative echocardiogram assessment. Indeed, the preoperative PL angle had a very high sensitivity and specificity to predict persistent MR early after operation. This parameter also was very powerful in predicting longer-term outcomes. Hence, 12 of the 13 patients with this finding developed ≥3/4 MR and, correspondingly, had New York Heart Association functional class ≥III/IV (Table 4). Three-year event-free survival in these patients also was much lower than in the rest of the cohort (22±17% versus 76±12%, P<0.001).

In contrast, perioperative assessment of MR severity by transesophageal echocardiography immediately after the realization of MVA was not helpful in predicting the persistence of MR and/or outcome after operation. These results are consistent with previous studies showing that perioperative transesophageal echocardiography generally underestimates ischemic MR severity and has a relatively low performance to predict early or late recurrence of MR after surgery.16
Mechanism of Persistent Ischemic MR

The results of the present study are in accordance with both fundamental and clinical studies that have examined the potential mechanism(s) of ischemic MR and its persistence after restrictive MVA. Green et al.\textsuperscript{12} have shown, in an ovine model, that MVA considerably reduces the mobility of the PL and transforms the mitral valve in a unicuspid valve, where valve closing is performed only by the anterior leaflet. Similarly, Matsunaga et al.\textsuperscript{13} have reported that annuloplasty does not protect against recurrent MR in patients with severe alteration of mitral valve geometry, such as severe displacement of posterior papillary muscle and important systolic apical traction of the leaflet. Zhu et al.\textsuperscript{10} have proposed that the persistence of significant MR after MVA is attributable to persistent tethering of both leaflets with predominant increases in PL tethering. The results of the study by Kuwahara et al.\textsuperscript{17} also suggest that this mechanism may be implicated not only in the persistence of MR immediately after restrictive annuloplasty but also in the recurrence of MR thereafter.

The fact that the PL angle was superior to other indices of valve geometry in predicting outcomes can likely be explained in light of the aforementioned findings as well as those reported by Agricola et al.\textsuperscript{18} Indeed, these authors describe 2 patterns of valve leaflet tethering that are essentially determined by the type of LV remodeling. Hence, approximately 59% of patients in their study had asymmetric tethering attributable to local LV remodeling, and these patients were characterized by increased restriction of PL, whereas 41% of patients had symmetric tethering of both leaflets associated with global LV remodeling. Interestingly, the common denominator of these 2 patterns is the presence of PL restriction with anterior leaflet restriction (symmetric tethering) or without anterior leaflet restriction (asymmetric tethering) (Figure 5). Likewise, in the present study, excessive LV dilatation was observed in 8 of the 11 patients with persistent MR; in addition to a PL angle $\geq 45^\circ$, these patients also had concomitant tenting area $\geq 2.5$ cm$^2$ and coaptation distance $\geq 1.0$ cm (Figure 3), consistent with a pattern of symmetric tethering and also consistent with the study of Calafiore et al.\textsuperscript{19} showing that a coaptation distance $\geq 1.1$ cm is associated with a high risk of MR recurrence after MVA. Nonetheless, the 3 patients who had persistent MR without LV dilatation presented only PL restriction, without concomitant high tenting area or increased coaptation distance consistent with an asymmetric pattern of tethering. Hence, our results suggest that, in the presence of important PL restriction, restrictive annuloplasty may worsen the PL tethering and lead to persistent MR, regardless of the type of LV remodeling and/or leaflet tethering pattern (Figure 5), and the common denominator in all cases is severe tethering of the PL. Nonetheless, anterior leaflet restriction—and, alternatively, as shown in Figure 5, slippage relative to a restricted PL—should not be overlooked in understanding and repairing

![Figure 3. Comparison of the performance of 4-chamber posterior leaflet angle (A), tenting area (B), and coaptation distance (C) to differentiate nonpersistent mitral regurgitation patients from persistent mitral regurgitation patients. PPV indicates positive predictive value; NPV, negative predictive value.](http://circ.ahajournals.org/)

![Figure 4. Event-free survival after mitral valve annuloplasty among patients with ischemic mitral regurgitation according to the preoperative posterior leaflet angle. Numbers at the bottom indicate the number of patients at risk for each follow-up time in the studied groups.](http://circ.ahajournals.org/)
mitral valve tethering. The consideration of the anterior leaflet angle in combination with the other indices of mitral valve morphology may be useful to guide the operative strategy, especially in patients with global LV remodeling and symmetric tethering.

Reduced closing forces after annuloplasty also have been proposed to potentially explain persistent MR.\textsuperscript{20} The results of our present study do not, however, support this hypothesis. Indeed, we observed no significant difference between the persistent and nonpersistent MR groups regarding preoperative or postoperative closing forces index. Also, this parameter did not correlate with postoperative MR severity. We found that a larger mitral prosthesis ring was an independent risk factor for worse postoperative MR severity, but this factor accounted for only 5% of the variance of MR severity ($R^2=0.05$, $P=0.02$) compared with 55% for the parameters of preoperative mitral valve configuration ($R^2=0.47$, $P<0.001$ for PL angle; $R^2=0.08$, $P=0.003$ for coaptation distance).

**Clinical Implications**

The prevalence of persistent MR observed in the present study (22%) is quite high and is consistent with that reported by Zhu et al\textsuperscript{10} (19% of mild to moderate MR). More recently, Serri et al\textsuperscript{11} have reported a prevalence of 11% of persistent MR. The lower prevalence found by these investigators may be attributable to the fact that they used a semiquantitative visual estimation method to assess MR severity (whereas we used a quantitative method [ie, vena contracta width]) or to a difference in the baseline characteristics of patients.

Moreover, persistent MR, even if mild to moderate at the outset, was associated with much worse clinical outcomes (Table 4). This finding is also consistent with recent studies.\textsuperscript{9,11} A probable explanation for the poorer outcomes is that persistent MR, even if mild, likely contributes to further deterioration of LV geometry, thus entailing more severe MR and creating a vicious circle, whereby more severe MR begets worse geometry, and vice versa.\textsuperscript{14}

The clinical implications of the present study are important because they suggest that the patients with the worst out-
comes after MVA for ischemic MR can prospectively be identified on the basis of preoperative echocardiograms. Hence, our results show that the procedure is most likely to fail in patients with a PL angle ≥45 degrees; in such patients, concomitant or alternative procedures should be contemplated. In this regard, there are presently many research efforts to find procedures that can improve LV geometry and, thus, enable the treatment of ischemic MR on the basis of its causal mechanism.18-21 Meanwhile, a better case scenario in patients with a PL angle ≥45 degrees would probably be mitral valve replacement with chordal sparing. In this respect, the patients with PL angle ≥45 degrees who underwent mitral valve replacement in our prospective series had no events and returned in functional New York Heart Association class II during follow-up (Table 4). On the other hand, a more restrictive annuloplasty with downsizing of more than 2 sizes in these patients would likely have worsened PL angulation and been unable to restore adequate leaflet coaptation (Figure 5).

Limitations
The main limitation of the present study is its retrospective design. It is possible that unidentified factors might have influenced the results. Nonetheless, our results show that the persistence of MR could have been predicted before operation in the vast majority of patients from the echocardiographic assessment of mitral valve configuration.

Another limitation is that MR severity was quantitatively evaluated only with the use of vena contracta width and not by proximal isovelocity surface area or volumetric methods. A previous study, however, had demonstrated that vena contracta width is a simple, accurate method to assess regurgitation severity.25 In this regard, Lesniki-Sobelga et al26 have shown excellent correlations between vena contracta width and effective regurgitant orifice area (r=0.85), regurgitant volume (r=0.85), regurgitant fraction (r=0.84), and angiographic grade (r=0.85). Moreover, the fact that the persistence of MR defined on the basis of vena contracta width was associated with markedly worse clinical outcomes further corroborates the validity of this method for the assessment of MR severity.

Clinical experience shows that reliance on a single quantitative echocardiographic parameter often entails potential pitfalls and limitations. Hence, we caution that measurement of PL angle requires good-quality tracings and may be subject to a certain learning curve. The consideration of other indices such as coaptation distance, tenting area, and anterior leaflet angle may be useful to obtain a more comprehensive evaluation of mitral valve morphology. Moreover, 3-dimensional echocardiography could contribute to improve the feasibility and accuracy of the measurement of these indices and, particularly, of PL angle.

Conclusion
The results of the present study show that the postoperative persistence of MR can be predicted from the preoperative analysis of the mitral valve configuration by transthoracic echocardiography. Patients with a preoperative PL angle ≥45 degrees are at very high risk for MR persistence and worse outcomes when treated by restrictive annuloplasty and CABG. In these patients, alternative or concomitant procedures should be considered. Procedures aimed at restoring ventricular geometry seem promising, but they require further investigation. In the meantime, mitral valve replacement with chordal sparing may be the preferred approach in these patients.

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Disclosures
None.

References
Ischemic mitral regurgitation often persists or recurs after restrictive mitral valve annuloplasty and adversely affects patient outcomes. The clinical implications of the present study are important because the present study demonstrates that the postoperative persistence of ischemic mitral regurgitation and 3-year event-free survival can accurately be predicted by preoperative analysis of mitral valve configuration by transthoracic echocardiography. In particular, the results show that mitral valve annuloplasty is most likely to fail in patients with a posterior leaflet (PL) angle $\geq 45$ degrees (i.e., with high PL restriction) and, furthermore, that this preoperative echocardiographic feature is associated with an extremely poor postoperative outcome. In these patients, restrictive annuloplasty may further worsen PL angulation and, thus, not restore adequate leaflet coaptation. Hence, patients with a PL angle $\geq 45$ degrees should be considered poor candidates for this procedure, and in such patients, concomitant or alternative procedures should be contemplated. In this regard, the results of the present study provide strong impetus for the development and validation of newer procedures that can improve left ventricular geometry and allow the treatment of ischemic mitral regurgitation on the basis of its causal mechanism. Pending validation of these new procedures, the best alternative for patients with high PL restriction would seem to be mitral valve replacement with chordal sparing. Hence, preoperative echocardiographic measure of PL angle can be useful to guide the surgical strategy for the treatment of ischemic mitral regurgitation and should, therefore, be incorporated into the clinical decision-making process.
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