



ADULT CARDIAC SURGERY:

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Changes in Mitral Regurgitation After Replacement of the Stenotic Aortic Valve

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Background. Concomitant mitral regurgitation (MR) is frequently seen in patients undergoing aortic valve replacement (AVR) for aortic stenosis. This study was undertaken to characterize the magnitude of MR in these patients and identify factors associated with significant postoperative change.

Methods. Between 2002 and 2006, 391 patients with stenotic AV disease but no structural mitral valve disease underwent AVR without coronary artery bypass grafting. Excluded were 164 patients with combined aortic and mitral intervention, right heart surgery, or moderate to severe aortic insufficiency, to yield a final study group of 227 patients. Follow-up echographic evaluation of MR was obtained in 87 of 219 patients (40%) discharged alive without mitral valve intervention.

Results. Overall mortality was 3.5%. After AVR, intraoperative MR severity improved in 66% of patients. Independent predictors of lower postoperative MR were

small left atrial size ($p = 0.03$), the presence of aortic insufficiency ($p < 0.01$), and preoperative congestive heart failure ($p = 0.04$). Prosthetic valve type or size was not an independent predictor of postoperative MR. After adjustment for intraoperative underestimation of MR grade, there was no difference between the postprocedural MR grade and the early or late follow-up MR grade ($p = 0.6$ and $p = 0.8$, respectively).

Conclusions. The results of this study support a conservative, tailored approach to concomitant mitral surgery in patients presenting for correction of aortic stenosis who demonstrate functional mitral regurgitation. Characteristics associated with resolution may allow for identification of patients most likely to benefit from mitral valve repair or replacement.

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Patients who require surgical treatment of aortic stenosis often present with concomitant mitral regurgitation (MR). When the MR is severe, a double-valve operation with mitral valve repair or replacement is indicated. In most patients, MR is less severe and surgical decision making is influenced by an expectation that there will be a reduction in MR with relief of the gradient across the aortic valve (AV) [1].

Limited data exists on the incidence and resolution of secondary or “functional” MR in patients presenting with aortic stenosis. The objective of this study was to characterize the prevalence of concomitant MR and factors associated with its resolution.

Patients and Methods

Study Group

Full approval and a waiver for patient consent were granted from the Institutional Review Board before the

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initiation of this study in July 2006. Patients undergoing aortic valve replacement (AVR) for aortic stenosis at Massachusetts General Hospital Heart Center between January 1, 2002, and January 1, 2006, were identified by query of our data warehouse.

Patients with normal valve leaflets or otherwise normally functioning mitral valves despite mild calcification of the posterior annulus or leaflet were included in the study and were defined as having secondary or “functional” MR. We also included patients who underwent AVR with concomitant aortic annular enlargement procedures and atrial septal defect repairs. We excluded patients with structural mitral valve disease, mitral stenosis, combined procedures involving coronary artery bypass grafting (CABG), treatment of endocarditis, right heart valve procedures, and patients with a preoperative diagnosis of moderate or severe aortic insufficiency (AI) so that patients presenting with aortic stenosis as the primary indication for intervention were selected.

Preoperative, operative, and immediate postoperative data were obtained from a repository containing validated data elements through an internal auditing process. Additional information was obtained by review of

Table 1. Preoperative Characteristics of 227 Patients Undergoing Isolated Aortic Valve Replacement

Patient Characteristics	No. (%) or Mean ± SD
Age, years	71 ± 11
Body surface area, m ²	1.9 ± 0.26
Female	125 (55)
Congestive heart failure	61 (27)
Atrial fibrillation	57 (25)
Angina	93 (41)
History of MI	18 (8)
NYHA class III/IV	114 (50)
Urgent status	85 (37)
Hypertension	162 (71)
Dyslipidemia	142 (63)
Peripheral vascular disease	16 (7)
Diabetes	47 (21)
Chronic lung disease	9 (4)
Renal failure	21 (9)
LVEF [5]	0.60 ± 0.14
AV gradient, mm Hg	51 ± 18
PA pressure, mm Hg	25 ± 9
Left atrial size, cm	4.3 ± 0.64
LV internal diameter, cm	4.7 ± 0.74
LV wall thickness, cm	1.3 ± 0.2
Vena contracta width, ^a cm	0.36 ± 0.11

^a Indicates the severity of mitral regurgitation (MR) as previously defined: VCW < 0.3, mild MR; VCW ≥ 0.7, severe MR.

AV = aortic valve; LA = left atrial; LV = left ventricle; LVEF = left ventricular ejection fraction; MI = myocardial infarction; NYHA = New York Heart Association; PA = pulmonary artery; SD = standard deviation.

the intraoperative echocardiograms. Patient mortality was defined as death within 30 days of operation. Morbidities were defined by The Society of Thoracic Surgeons data definitions document (version 2.51.1) [2]. Echocardiographic follow-up was obtained by querying the institutional echocardiographic database, patient records, and correspondence from referring cardiologists.

Table 2. Surgical Mortality and Morbidity in 227 Patients Undergoing Isolated Aortic Valve Replacement

Postoperative Course	No. (%)
30-day mortality	8 (3.5)
Reintubation	11 (4.8)
Reoperation ^a	17 (7.5)
New heart block requiring a pacemaker	9 (3.9)
Cardiac arrest	6 (2.6)
Post-op atrial fibrillation	69 (30)
Cardiac tamponade	4 (1.8)
Post-op stroke (>72 hours)	6 (2.6)
Pneumonia	6 (2.6)
New post-op renal dialysis required	3 (1.3)

^a Reoperation for complications related to bleeding/tamponade, cardiac reasons, and noncardiac reasons.

Table 3. Patient and Operative Characteristics Related to Risk of Death in 227 Patients Undergoing Isolated Aortic Valve Replacement

Characteristic	p Value	
	Univariable ^a	Multivariable ^b
High pre-op creatinine levels	<0.0001	<0.0001
Chronic lung disease	<0.0001	<0.0001
Lower ejection fraction	0.04	0.04
Dialysis	0.06	<0.0001

^a P values obtained using χ^2 statistics. ^b P values obtained using multivariate logistic regression analysis.

Echocardiography

Intraoperative, two-dimensional transesophageal echocardiography (TEE) was performed in all patients. Omniplane-3 Ultra-Band (Hewlett-Packard, Andover, MA) TEE probe (frequency, 2 to 7 MHz) transducers connected to Philips Sonos 5500 (Philips Medical Systems, NA, Bothell, WA) standard echocardiography consoles were used to perform the TEE studies. Previously recorded images were used to quantitatively assess the severity of functional MR immediately before and after surgical intervention. All measurements and assessments were performed on patients under general anesthesia.

One appropriately trained observer (E. W.) reviewed all echocardiograms. These results were verified by two expert echocardiographers (E. A., M. A.) to confirm accuracy. In addition to preoperative and postoperative MR grade, measurements were made of left atrial size, left ventricular wall thickness, and left ventricular internal diameter. The severity of MR was measured using the vena contracta method, as previously described [3].

The American Society of Echocardiography guidelines for evaluation of the severity of MR state that a vena contracta width (VCW) of less than 0.3 cm is considered a mild lesion, and a VCW of 0.7 cm or more is severe [4]. Values within these parameters are moderate lesions. A midesophageal 4-chamber view (transducer angle, 0° to 20°) and the midesophageal long-axis view (transducer angle, 120° to 135°) were used to obtain the VCW mea-

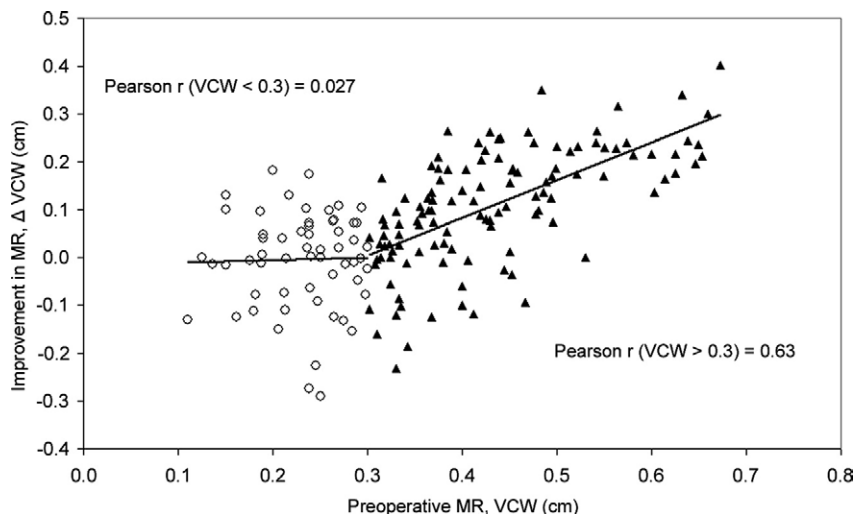
Table 4. Preoperative and Postoperative Mitral Regurgitation for Patients Undergoing Isolated Aortic Valve Replacement

Pre-op MR	Post-op MR		
	None-Mild (n = 157)	Moderate (n = 69)	Severe (n = 1)
None-Mild (n = 60)	46 (77%)	13 (22%)	1 (2%)
Moderate (n = 167)	111 (66%)	56 (34%)	...
Severe (n = 0)

Mild, moderate, and severe MR is defined as vena contracta width <0.3 cm, 0.3 to 0.7 cm, and ≥ 0.7 cm, respectively. Number values represent the number of patients from the appropriate preoperative category (row) that fall into the corresponding postoperative MR category (column). Parenthetical values represent the percentage of preoperative MR patients (row) who fall in the corresponding postoperative MR category (column).

MR = mitral regurgitation.

Fig 1. Association between preoperative mitral regurgitation (MR, x axis) and postoperative MR improvement (y axis) after isolated aortic valve replacement. Open circles represent mild preoperative MR (vena contracta width [VCW] <0.3 cm). Triangles represent greater than mild preoperative MR (VCW \geq 0.3).



surements. Left atrial size was measured from the midesophageal 4-chamber view from the lateral wall to the interatrial septum, and inferior left ventricular wall thickness and internal diameter were measured from the transgastric, short-axis view at end-diastole. Trabeculae carnea and papillary muscles were excluded for wall thickness measurements. At least three measurements were taken, and the mean value was calculated [5].

Aortic Valve Orifice Area

The in vivo valve area for the prosthetic AV was estimated using the effective orifice area (EOA) and geometric orifice area (GOA) of the valve prosthesis. The EOA was derived from the manufacturer's published values of projected in vivo EOA. This value was indexed to body surface area to yield the indexed effective orifice area (iEOA) of the valve. The GOA was also considered as a potentially important variable. It was calculated using the internal diameter of the valve ($GOA = \pi \times \text{inner ring radius}^2$). Indexing to the body surface area yielded the indexed geometric orifice area (iGOA) [6].

For the purposes of seeking relationships in valve size selection and outcomes, including resolution of MR, the iEOA and iGOA were both considered to be continuous variables. To facilitate tabular representation, an iEOA of less than $0.65 \text{ cm}^2/\text{m}^2$ and an iGOA of less than $1.2 \text{ cm}^2/\text{m}^2$ were defined as "patient-prosthesis mismatch"

Table 5. Independent Predictors of a Lower Postoperative Mitral Regurgitation in Patients Undergoing Isolated Aortic Valve Replacement

Characteristic	Multivariable ^a p Value
Preoperative MR (less)	<0.0001
Trace or mild AI (presence of)	0.01
Left atrial size (<4.5 cm)	0.03
Congestive heart failure	0.04

^a Values obtained using regression analysis (see Methods).

AI = aortic insufficiency; MR = mitral regurgitation.

in the present study [7–9]. EOA and GOA values used in this study were consistent with those used in other studies (Appendix) [10].

Statistical Analysis

The data are summarized as means \pm standard deviation or numbers and percentages. The Student *t* test was used to compare continuous variables between the groups, and χ^2 analysis of binary variables was performed. Logistic multivariable regression analysis with stepwise forward selection was used for binary outcomes, and linear multivariable regression was used for modeling of continuous outcomes. Criteria for entry and retention into multivariable models were set at the 0.1 and 0.05 confidence level, respectively. Only variables significant at the 0.1 level were considered for the multivariable analyses.

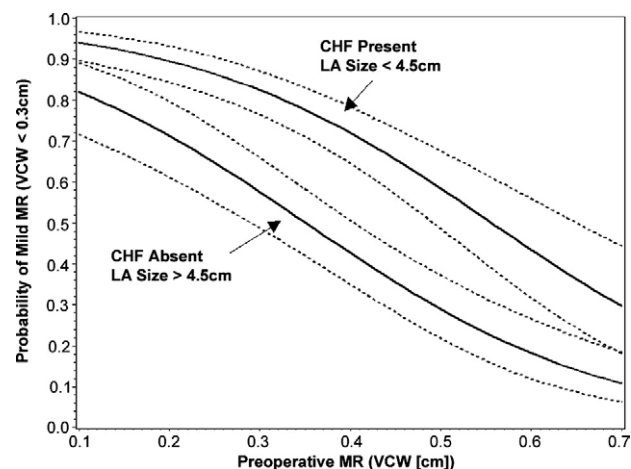


Fig 2. The probability of a patient leaving the operating room with mild or less mitral regurgitation (MR), defined as vena contracta width (VCW) <0.3 cm, as a function of preoperative MR, congestive heart failure (CHF), and left atrial (LA) size. Solid lines represent solutions to the multivariable model regression equation for postoperative MR, and dashed lines are the corresponding 70% confidence limits (see Table 5).

A second logistic regression analysis was conducted to determine the factors associated with achieving postoperative mild MR. For this analysis, the 227 patients with isolated AVR were considered. A depiction was created from the regression equation, and 70% confidence intervals were applied. For multivariable analysis, missing data or variables were standardized to the mean of the known group.

In a secondary exploratory analysis, we assessed the pattern of change in mitral valve regurgitation grade for 87 patients (40%) discharged alive who had no procedure performed on the mitral valve and in whom we were able to obtain follow-up echocardiography evaluation of the mitral valve. To be consistent with follow-up echocardiography reports, mitral valve regurgitation grade was defined in four categories as none/trace, mild, moderate, and severe. A mixed-effects ordinal logistic regression model [11] was used to account for the correlation between repeated echocardiography measurements and was calculated using the NLMIXED procedure in SAS 9.1 software (SAS Institute, Cary, NC). We defined five time points for echocardiography measurements: baseline (preoperative), intraoperative preprocedure, intraoperative postprocedure, early follow-up (<30 days), and late follow-up (700 ± 506 days). Values of $p < 0.05$ were considered to be statistically significant.

Results

Patient Population

From the Massachusetts General Hospital Cardiac Data Warehouse, 391 patients without structural mitral valve pathology who underwent AVR without CABG from January 1, 2002, to January 1, 2006, were identified. From this cohort, 29 patients were excluded for the following reasons: endocarditis, concomitant pulmonic or tricuspid operations, or procedures for ascending aortic pathology. Because the main objective of this study was to assess change in MR when no procedure was performed on the mitral valve, 7 patients who underwent AVR plus mitral valve replacement and 7 who had repair were excluded. Also excluded were 121 patients with preoperative moderate or severe AI, leaving 106 patients with mild AI and 121 patients with either none or only trace AI. Preoperative, intraoperative, and echocardiographic characteristics are listed in Table 1. Of note, no patient presented with hypertrophic obstructive cardiomyopathy.

Morbidity and Mortality

Morbidity and mortality are reported in Table 2. Preoperative and intraoperative variables were analyzed to determine univariable and multivariable associations with death (Table 3).

Factors Associated With Resolution of MR

After AVR, the degree of MR improved in 112 of 227 patients (649%). Of the 167 patients preoperatively diagnosed with moderate MR, the regurgitation improved postoperatively in 111 (66%). Postoperative change in MR is reported in Table 4 and Figure 1.

When observed MR was mild or less, there was a weak correlation ($p = 0.8$, Pearson $r = 0.027$) between preoperative MR and postoperative MR (Fig 1). However, when the MR was more than mild, there was a strong, linear correlation ($p < 0.0001$, Pearson $r = 0.63$). By multivariate analysis, independent predictors of the degree of MR after isolated AVR are listed in Table 5. Figure 2 depicts the probability of preoperative MR resolving to a degree classified as “mild” (VCW < 0.3 cm) after isolated AVR by grouping patients into two groups; those with congestive heart failure (CHF) who did not have an enlarged left atrium (<4.5 cm), and those without CHF who presented with an enlarged left atrium (>4.5 cm).

Impact of Aortic Prosthesis Size

According to our definitions of “patient-prosthesis mismatch,” (iEOA < 0.65 cm²/m² and an iGOA < 1.2 cm²/m²), 7 patients had a mismatch according to iEOA, 8 had a mismatch according to iGOA, and only 3 had mismatch according to both definitions. No independent relationship was found between prosthesis size and change in MR considering both iGOA and iEOA as continuous measures ($p = 0.2$, Pearson $r = 0.095$). An aortic root enlargement procedure was performed on 11 patients (4.6%), all of whom underwent isolated AVR, and their mortality, morbidity and change in concomitant MR were not significantly different than the overall group.

Early and Late Follow-Up Change in MR

Amongst the 87 patients (40%) discharged alive who had no procedure performed on the mitral valve and in whom late echocardiographic information was available, the relationship of pre- and postoperative transthoracic echocardiographic (TTE) to intraoperative transesophageal echocardiographic (TEE) assessment of MR was investigated. In this group, more patients presented moderate MR in the preoperative TTE (19.9%) compared with the intraoperative preprocedural TEE (9.9%) (odds ratio [95% confidence interval]: 3.28 [1.65–6.52]; $p = 0.01$). The intraoperative underestimation of MR grade was estimated by the preoperative–intraoperative preprocedural difference in the MR grade. After adjustment for this underestimation, there was no difference between the postprocedural presence of moderate MR (7.1% by TEE) and the early (OR 0.74 [0.23–2.40]; $p = 0.6$) or late (OR 1.15 [0.42–3.13]; $p = 0.8$) follow-up presence of moderate MR. Moreover, the MR grade did not progress to “severe” in any patient during early or late follow-up.

Comment

Physiologic changes caused by aortic stenosis can create or magnify functional MR. In addition to the direct gradient effect on ventricular systolic pressures, remodeling, hypertrophy, and fluid overload can also aggravate MR [12]. As a result, a high incidence of primary aortic stenosis patients present with significant secondary MR. In the current series of patients, 75% had at least moderate preoperative MR.

Decisions regarding surgical treatment are challenging

given incomplete information. Without mitral intervention, there is evidence to suggest that relief of the AV gradient alone should cause immediate improvement in left ventricular pressure, with some reduction in MR. Additional benefit may be achieved over time with regression of left ventricular hypertrophy and resolution of volume overload. Avoiding unnecessary additional operations in these patients may reduce morbidity, especially given the sensitivity of the hypertrophied heart to ischemia.

Despite these observations, some groups recommend an aggressive approach to operating on the mitral valve. Supporting this idea is the observation that double-valve operations for aortic stenosis and secondary MR are low risk and have impressive results [12]. The use of aggressive therapy is further supported by data showing that concomitant moderate to severe MR does not improve in half the patients and that it is increased in a small subgroup of patients [13–15]. Another study observed that no difference in survival, but isolated AVR for patients with preoperative MR exceeding 2 had increased composite end points of CHF and reintervention. These authors identified several important risk factors, including left atrial size exceeding 5 cm, AV gradient of less than 60 mm Hg, and atrial fibrillation [16]. On the other extreme, some believe that repair or replacement is unnecessary unless patients clearly demonstrate severe MR. Several reports have documented minimal or no impact on early morbidity when there is no intervention on the mitral valve [1, 17–19].

Other recent reports have included patients with mixed mitral pathology, or concomitant CABG [20]. These factors may complicate the interpretation of changes in MR in the isolated AVR population. In a previous analysis, we documented a reduction in MR by CABG alone [21]. In the case of patients with structural mitral valve disease, it is generally known that the degree of benefit from isolated AVR will be limited, and we did not include this population in the present study.

In an attempt to provide information for surgical decision making, the current analysis identified several characteristics that were independently associated with changes in MR:

- Left atrial size. Our analysis underscores the importance of left atrial size as a predictor of postoperative MR (Table 5). Left atrial enlargement is a chronic change and is not only a surrogate marker of the chronicity of disease but is also highly correlated with atrial fibrillation and older age, and is an important predictor of postoperative death [22].
- Congestive heart failure. Patients presenting with CHF enjoyed a greater resolution of MR. The designation of a patient as having CHF in this study implies the presence of symptoms of failure (fluid overload) within 2 weeks of operation, as defined by The Society of Thoracic Surgeons [2]. Does the MR contribute to the CHF, or does the aortic stenosis-induced CHF cause increased MR? The causal mechanism at play is critical for the

surgical care of these patients. This study supports the latter, implying that one can reliably expect greater improvement in MR in patients presenting with fluid overload by performing only an AVR. The MR in CHF patients would appear to be due, at least in substantial part, to the advanced aortic stenosis. In addition, preoperative fluid management for MR cannot be optimized in patients presenting with aortic stenosis as it would be for a patient with CHF but no aortic stenosis. The immediate resolution of MR is likely due not only to the relief of gradient but also to the reduction in fluid status by intraoperative modulation of intravascular pressures and hemoconcentration on bypass.

- Atrial fibrillation. Although not specifically identified as an independent predictor, the relationship of this condition with left atrial size ($p = 0.02$), CHF ($p < 0.001$), and age ($p < 0.001$) are worth noting. Patients with atrial fibrillation are less likely to see improvement in MR ($p = 0.1$). This effect is accounted for by the presence of correlated variables.
- Aortic insufficiency. Although patients with moderate or severe AI were excluded, we did include patients with mild AI because we believed that they would be part of a representative population of patients whose primary indication was aortic stenosis. Mild AI in this setting is not generally considered to be physiologically significant. Somewhat unexpectedly, we identified that these patients with trace or mild AI had more improvement in postoperative MR than would otherwise be expected. The mechanism leading to this relationship is unclear. Certainly, the AI causes increased end-diastolic ventricular volume, but at this degree, its significance was not expected. It is also possible that patients with symptomatic aortic stenosis have underestimated AI due to a combination of use of angiotensin-converting enzyme inhibitors and diuretics. If the underestimated AI is resolved along with the aortic stenosis, a notable improvement of MR severity in these patients may be observed.

It has previously been argued that the concept of patient-prosthesis mismatch may affect the success of corrective AV operations [7, 8, 23]. Our study supports previous work documenting the lack of relationship between indexed valve size with death and postoperative functional recovery [24, 25]. The choice of valve size did not appear to impact the resolution of MR. In addition, iEOA was not associated with increased early death nor was it an independent risk factor by multivariable analysis. Performance of aortic root enlargement was unrelated to the risk of death or reduction in MR in our small study population.

Previous studies have used categorical measurements of MR that have been less precise than those used in this study. Because categorical classifications are often too coarse to allow optimal decision making and are prone to observer error and bias, it is important for the surgeon to

obtain a quantitative assessment of MR. Our approach was to measure the degree of MR using the VCW method, which has been validated with TEE and is an accepted method that provides an accurate quantitative assessment of the degree of MR for both central and eccentric jets [3, 5, 25]. The VCW is especially appropriate in the operative setting because its accuracy is less dependent on loading conditions [3, 4, 26].

The principal limitation of this study is that it is primarily based on an intraoperative assessment of the MR, with limited postoperative follow-up data. Previous reports have demonstrated that echocardiographic data obtained 10 minutes postoperatively were comparable with data acquired after 1 day [25]. We recognize that the remodeling that occurs after AVR may lead to delayed changes that cannot be immediately observed. Late changes in preload or afterload associated with general anesthesia are additional limitations to interpretation of this study.

In addition, variability of quality and completeness of the recorded echocardiographic studies limited our ability to obtain a complete set of all four desired echocardiographic measurements in 20% of the patients. In these patients, the echocardiographic results did not allow a full set of variables because the goal was to extract the maximum amount of data without including data that were not clearly recorded. As a retrospective study, follow-up echocardiography measurements were incomplete and opportunistic. These were performed in the context of a routine follow-up by the referring cardiologist. Given that an echocardiographic examination may be more likely in the context of unexpected physical examination findings or clinical course, this may represent a biased sample of the overall study population. If so, this bias should tend to make regurgitation appear more likely than it would be in a complete sample.

In conclusion, the results of this study support a conservative, tailored approach to concomitant mitral surgery in patients presenting for correction of aortic stenosis who demonstrate functional regurgitation. Mitral annuloplasty or replacement appears warranted in patients with severe regurgitation. Mitral operations may be avoided in essentially all cases of mild regurgitation. For the large group of patients with moderate regurgitation, identified patient characteristics may aid in selection of patients for whom more aggressive surgical treatment is warranted.

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Appendix

Values Used for Geometric and Effective Orifice Areas of the Aortic Prosthetic Valves

Valve Size	Valve Name	No.	GOA (cm ²)	pEOA (cm ²)
17	St. Jude Medical Hemodynamic Plus 505 ^a	1	1.70	1.16
19	Carpentier-Edwards 2800 ^b	24	2.54	1.22
	Carpentier-Edwards Standard Porcine 2625	3	2.27	.90
	Carpentier-Edwards Perimount Magna 3000	5	2.54	1.50
21	St. Jude Medical Standard 502	1	1.70	1.01
	Carpentier-Edwards 2800	65	3.14	1.52
	Carpentier-Edwards Perimount Magna 3000	14	3.14	1.82
	Carpentier-Edwards Standard Porcine 2625	6	2.83	1.30
	Carbomedics Top Hat ^c	1	2.19	1.18
	Medtronic-Hall 7700 ^d	1	2.01	1.56
	St. Jude Medical Standard 502	10	2.19	1.33
	Medtronic Freestyle 995	3	2.54	1.20
	Medtronic Mosaic 305	1	2.69	1.20
22	Medtronic-Hall 7700	2	2.54	1.56
23	Carpentier-Edwards 2800	40	3.80	1.75
	Carbomedics Top Hat	1	2.69	1.37
	St. Jude Medical Standard 502	7	2.69	1.60
	Carpentier-Edwards Standard Porcine 2625	8	3.46	1.60
	Carpentier-Edwards Perimount Magna 3000	11	3.80	1.96
	Medtronic Mosaic 305	1	3.30	1.60
	St. Jude Medical Hemodynamic Plus 505	1	3.27	2.59
25	Carpentier-Edwards 2800	26	4.52	1.80
	Carpentier-Edwards Standard Porcine 2625	6	4.15	1.75
	Carpentier-Edwards Perimount Magna 3000	1	4.52	2.12
	Medtronic Mosaic 305	2	3.97	1.90
	St. Jude Medical Standard 502	4	3.27	1.93
27	Carpentier-Edwards Standard Porcine 2625	1	4.91	2.40
	St. Jude Medical Standard 502	5	3.90	2.35
31	St. Jude Medical Standard 502	1	5.31	3.08

^a St. Jude Medical, St Paul, MN. ^b Carpentier-Edwards, Irvine, CA. ^c Carbomedics, Austin, TX. ^d Medtronic, Minneapolis, MN.

GOA = geometric orifice area, which is calculated as $GOA = \pi \times (\text{valve radius})^2$; pEOA = projected effective orifice area—in vivo measurement of EOA obtained from the manufacturer.