Patient survival characteristics after routine mitral valve repair for ischemic mitral regurgitation

Donald D. Glower, MD^a
Robert H. Tuttle, MSPH^a
Linda K. Shaw, MS^a
Ricardo E. Orozco^{b,c}
J. Scott Rankin, MD^{b,c}

Background: Ischemic mitral regurgitation has been associated with diminished survival compared with nonischemic mitral regurgitation. Conversion from mitral valve replacement to valve repair has improved prognosis, but it is unclear whether ischemic mitral regurgitation remains an independent predictor of outcome after mitral valve repair.

Methods: Five hundred thirty-five patients undergoing mitral valve repair (primarily rigid ring annuloplasty) with or without coronary bypass from 1993 through 2002 were reviewed retrospectively (ischemic mitral regurgitation, $n = 141$; nonischemic mitral regurgitation, $n = 394$). A Cox proportional hazards model evaluated survival as a function of 9 simultaneous covariates: ischemic versus nonischemic mitral regurgitation, age, sex, number of medical comorbidities, ejection fraction, New York Heart Association class, coronary disease, reoperation, and year of operation.

Results: According to univariable analysis, patients with ischemic mitral regurgitation had greater age, higher comorbidity, lower ejection fraction, higher New York Heart Association, and higher reoperation rate (all $P < .001$) compared with those having nonischemic mitral regurgitation. Univariable 30-day mortality was as follows: 4.3% for patients with ischemic mitral regurgitation versus 1.3% for patients with nonischemic mitral regurgitation ($P = .01$). Unadjusted 5-year mortality was as follows: $44\% \pm 5\%$ for patients with ischemic mitral regurgitation versus $16\% \pm 3\%$ for patients with nonischemic mitral regurgitation ($P < .001$). In the multivariable model, however, only the number of preoperative comorbidities and advanced age were independent predictors of survival ($P < .0001$), whereas ischemic mitral regurgitation, sex, ejection fraction, New York Heart Association class, coronary disease, reoperation, and year of operation did not achieve significance (all $P > .19$). After being adjusted for differences in all preoperative risk factors, survival was not statistically different between ischemic mitral regurgitation and nonischemic mitral regurgitation ($P = .33$).

Conclusions: With routine application of rigid ring annuloplasty, long-term patient survival is more influenced by baseline patient characteristics and comorbidity than by ischemic cause of mitral regurgitation per se. Future risk assessment and decision making should be based on patient condition and should not be biased by ischemic cause of mitral regurgitation.

From Duke University Medical Center, Durham, NC^a; Centennial Medical Center, Nashville, Tenn^b; and Vanderbilt University, Nashville, Tenn.^c

Supported by a grant stipend from Edwards Lifesciences, LLC, to the Duke Clinical Research Institute.

Read at the Eighty-fourth Annual Meeting of The American Association for Thoracic Surgery, Toronto, Ontario, Canada, April 25-28, 2004.

Received for publication May 4, 2004; revisions received Oct 17, 2004; accepted for publication Nov 17, 2004.

Address for reprints: Donald D. Glower, MD, Duke University Medical Center, Box 3851, Durham, NC 27710 (E-mail: glowe001@mc.duke.edu).

J Thorac Cardiovasc Surg 2005;129:860-8
0022-5223/\$30.00

Copyright © 2005 by The American Association for Thoracic Surgery

doi:10.1016/j.jtcvs.2004.11.023

Mitral regurgitation (MR) precipitated by a myocardial infarction (ischemic MR [IMR]) significantly worsens the prognosis of patients with coronary artery disease.¹ Furthermore, surgical therapy for moderate-to-severe IMR has been associated with diminished early and late survival compared with nonischemic MR (NMR).²⁻⁷ As a result of the perception that the worse prognosis after surgical intervention for IMR is inherent to IMR itself, patients with IMR have been more reluctantly referred for operation than patients with NMR.^{3,4}

Although the results of mitral repair for IMR have improved over the last 20 years,^{2,8} ongoing dissatisfaction with outcomes has yielded many divergent approaches to IMR repair, including undersized flexible ring annuloplasty,⁹ selective valve replacement rather than repair,⁷ uniform chordal sparing valve replacement,¹⁰ transection of secondary chordae,¹¹ suture annuloplasty,¹² posterior leaflet patch extension,¹³ annular cinching,¹⁴ and papillary muscle sling.¹⁵ For the last decade, however, the authors have continued the consistent approach of routine rigid ring annuloplasty and complete coronary revascularization for the treatment of IMR. The present study was designed to examine the results of this management strategy and to assess the influence of IMR as an independent predictor of survival after mitral valve repair by multivariable regression modeling methods.

Methods

This series consisted of 535 consecutive patients undergoing mitral valve repair for mitral regurgitation with or without coronary artery bypass (CAB) by 2 surgeons at 2 institutions over a 9-year period from January 1, 1993, to December 31, 2002. Patients undergoing concurrent aortic, tricuspid, or pulmonic valvular procedures were excluded. Of these 535 patients, 141 had IMR, which was defined as the combination of (1) prior myocardial infarction, (2) 75% or greater stenosis of at least one coronary vessel, (3) a corresponding regional wall motion abnormality, and (4) absence of other mitral valve pathology, such as myxomatous prolapse or primary leaflet fibrosis. The remaining 394 patients were considered to have NMR, with the distribution of mitral valve cause being prolapse ($n = 290$), pure annular dilatation ($n = 74$), endocarditis ($n = 20$), or other ($n = 10$).

Selected patients not requiring CAB ($n = 247$) were approached with port-access technology,¹⁶ and the remainder received median sternotomy. The final decision to repair the mitral valve was based on observation of moderate-to-severe MR on the prebypass transesophageal echocardiogram, together with preoperative echocardiography or ventriculography.¹⁷ The majority of patients (524/535 [98%]) were managed with cardiopulmonary bypass and cold potassium cardioplegia, and the remainder (11/535 [2%]) underwent operations with hypothermic ventricular fibrillation caused by previous surgical intervention or patent bypass grafts. Most (529/535 [99%]) underwent rigid ring annuloplasty (Carpentier Classic, Carpentier Physio [Edwards Life-

sciences, Irvine, Calif], or Seguin [St Jude Medical, Inc, St Paul, Minn] rings) sized according to the intertrigonal distance. In most patients with IMR, the ring size was reduced by one size. Four patients with large posterior aneurysms were treated with transventricular mitral repair.¹⁸ Two patients, deemed too small for a 24-mm ring, underwent suture annuloplasty. Annuloplasty rings were inserted with interrupted horizontal mattress sutures buttressed with supra-annular pledgets, if needed, for additional strength. Leaflet prolapse in the NMR group was managed with various combinations of quadrangular or triangular resections, leaflet sliding plasties, or polytetrafluoroethylene artificial chordal replacements (Gore-Tex chordal replacement; W. L. Gore & Associates, Inc, Newark, Del).^{19,20} All coronary vessels of 1.5 mm in diameter or larger that were obstructed by 50% or greater were bypassed. Most patients receiving coronary bypass grafting had at least one internal thoracic artery inserted. Of patients with IMR treated over this period but excluded from this series, 10 required valve replacement: 1 for a ruptured large single posterior papillary muscle, 7 for concomitant fibrosis or calcification of the anterior leaflet, and 2 for prolapse caused by papillary muscle infarction.

After 1996, routine arrhythmia prophylaxis was used. Patients were intravenously loaded with amiodarone starting at least 12 hours before surgical intervention²⁰ or with procainamide intraoperatively. Oral therapy with amiodarone, sotalol, or other agents was continued for at least 3 to 6 weeks postoperatively. Maze operations or atrial ablations ($n = 27$) were used only selectively for patients with long-term preoperative atrial fibrillation.

Positive comorbidity of chronic lung disease was defined as severe emphysema requiring daily pharmacologic therapy, preoperative renal insufficiency was defined as a serum creatinine level of 1.5 mg/dL or greater, postoperative renal insufficiency was defined as an increase in serum creatinine level of greater than 1.0 mg/dL, severe left ventricular dysfunction was an estimated ejection fraction of 0.35 or less, a stroke was a permanent neurologic defect, and operative mortality was defined as death during hospitalization or within 30 days of surgical intervention. Of the 535 patients, 99% had confirmation of clinical status or personal contact by telephone in late 2002. Echocardiographic findings within 2 years of the follow-up date were documented. Maximal follow-up was 9 years, and median follow-up was 4 years.

Baseline characteristics were reported as percentages for discrete variables and compared by χ^2 tests; continuous variables were described by median, 25th, and 75th percentiles, with differences assessed by Kruskal-Wallis tests. Cumulative survivals as a function of time after the date of surgical intervention were generated by using the Kaplan-Meier method. The Cox proportional hazards model was used to examine both univariable and multivariable relationships between baseline characteristics and mortality by using stepwise selection of candidate variables at an α value of .05. The model evaluated long-term survival as a function of 9 simultaneous covariates: IMR versus NMR, age, sex, weighted count of comorbidities (hypertension, smoking, diabetes, renal insufficiency, pulmonary disease, peripheral vascular disease, and cerebral vascular disease weighted on the basis of the parameter estimates of these components in a separate Cox regression model), ejection fraction (EF), New York Heart Association (NYHA) class, coronary disease (CD), prior cardiac operation, institution, and year of operation. The Cox model assumption of

TABLE 1. Preoperative patient characteristics

	NMR	IMR	P value
N	394	141	
Age (y)	59 (51-69)	69 (61-75)	<.001
Female sex	170 (43%)	61 (43%)	.98
Hypertension	94 (24%)	55 (39%)	.001
Smoking	43 (11%)	30 (21%)	.002
Diabetes	30 (8%)	49 (35%)	<.001
Renal disease	26 (7%)	26 (18%)	<.001
Lung disease	33 (8%)	31 (22%)	<.001
Peripheral vascular	11 (3%)	17 (12%)	<.001
Cerebrovascular	19 (5%)	15 (11%)	.015
Ejection fraction	50 (40-56)	40 (30-43)	<.001
NYHA class			<.001
I	16 (4%)	3 (2%)	
II	73 (19%)	2 (1%)	
III	156 (40%)	35 (25%)	
IV	149 (38%)	101 (72%)	
Coronary disease	63 (16%)	141 (100%)	<.001
Prior operation	17 (4%)	28 (20%)	<.001
Concurrent CAB	63 (16%)	123 (87%)	<.001
Institution Duke	307 (78%)	110 (78%)	.99

Baseline characteristics of the NMR versus IMR groups are shown. Values shown in parentheses are 25th-75th percentiles for continuous variables. *NMR*, Nonischemic mitral regurgitation; *IMR*, ischemic mitral regurgitation; *NYHA*, New York Heart Association; *Prior operation*, previous cardiac operation; *CAB*, coronary artery bypass.

linearity in the log hazard was tested for all continuous and ordinal categorical variables, and they were transformed appropriately as needed. None of the variables violated the assumption of proportional hazards when tested in the Cox model. Potential collinearity of independent variables was minimized by use of a total count of comorbidities. Analysis was also repeated, including individual comorbidities instead of the total number of comorbidities. Because of concerns that CD and impaired EF could act as surrogates for IMR in the model, the analysis then was repeated with 8 variables plus CD and EF combined and then again with CD and EF omitted. Additionally, adjusted survival curves were generated to further evaluate the relationship between CD and cause, stratifying on cause in a CD-only subset population.

A propensity score analysis was performed to determine whether the differences between the IMR and NMR groups remained similar across different probabilities of the mitral valve disease cause by using preoperative variables to create propensity scores for the diagnosis of IMR versus NMR. After dividing all patients into 5 equal strata on the basis of the propensity for diagnosis of IMR, area under the survival curve was calculated for each quintile, and differences between cause groups were tested statistically. This study was approved by the Institutional Review Boards of Centennial Hospital (Nashville, Tenn) and Duke University (Durham, NC).

Results

Ring size was significantly smaller for patients with IMR versus patients with NMR (25th, 50th, and 75th percentiles:

24, 26, and 26 mm for IMR vs 26, 30, and 34 mm for NMR; $P < .0001$). Patients undergoing valve repair for IMR had greater age, higher comorbidity (hypertension, smoking, diabetes, renal insufficiency, lung disease, cerebrovascular disease, and peripheral vascular disease), lower EF, higher NYHA class, more CD, and a higher incidence of reoperation compared with patients undergoing valve repair for NMR (Table 1). No differences were observed in terms of sex or institution. Patients with IMR were more likely to undergo concurrent coronary bypass grafting (87% vs 16%). Severe left ventricular dysfunction ($EF \leq 0.35$) occurred in 9% (36/394) of patients with NMR but was observed in 37% (52/141) of patients with IMR ($P = .0001$). In the total population 31% were older than 70 years, and 7% were older than 80 years. Five patients had moderate-to-severe MR on preoperative or prebypass echocardiography, and the remaining 530 patients had severe MR. Class III and IV congestive heart failure or anginal symptoms were present preoperatively in 82% (441/535) of patients. Patients from the 2 different institutions had similar baseline characteristics, except that patients at Duke had more hypertension, smoking, diabetes, and vascular disease and had greater EF.

On postbypass transesophageal echocardiography, only 1 patient with IMR had more than mild MR after repair compared with 2 patients with NMR ($P =$ not significant). Unadjusted 30-day mortality was higher for patients with IMR (6/141 [4.3%]) versus those with NMR (5/394 [1.3%], $P = .04$). Unadjusted operative mortality was also higher for patients with IMR (9/141 [6.4%]) versus patients with NMR (5/394 [1.3%], $P = .01$). Causes of operative death for patients with IMR included ventricular arrhythmias in 3, sepsis in 2, respiratory failure in 2, mediastinitis in 1, pneumonia in 1, and low cardiac output in 1. For patients with NMR, death was caused by heparin-induced thrombosis in 1, sepsis in 1, stroke in 1, and liver failure in 1. Postoperative complications tended to be higher in patients with IMR (no. [%] with IMR vs no. [%] with NMR): stroke in 3 [2.1%] vs 5 [1.3%], renal failure in 10 [7.1%] vs 9 [2.3%], prolonged ventilation [>48 hours] in 8 [5.7%] vs 12 [3.0%], reoperation for bleeding in 3 [2.1%] vs 13 [3.3%], deep sternal infection in 1 [0.7%] vs 0 [0%], sepsis in 2 [1.4%] vs 1 [0.3%], gastrointestinal complications in 8 [5.7%] vs 13 [3.3%], and new pacemaker in 6 [4.3%] vs 7 [1.8%]. Median (25th-75th) postoperative stay was 8 days (6-11 days) for IMR and 6 days (5-8 days) for NMR ($P < .001$, Mann-Whitney test).

The results of locally available late postoperative echocardiograms were obtained in 58% (309/535) of patients (85/141 [60%] with IMR and 224/394 [57%] with NMR, $P = .5$). Late echocardiograms were not available in the remainder primarily because of absence of symptoms and murmurs. The median time (25th-75th) to last follow-up

Figure 1. Survival of patients undergoing mitral valve repair with IMR versus NMR (*No IMR*) before (A) and after (B) adjustment for differences in baseline patient characteristics.

echocardiogram was 1.4 years (0.1-3.1 years) for patients with IMR versus 1.8 years (0.3-4.3 years) for patients with NMR. Moderate or severe MR was documented to have recurred in 8% (30/394) of the NMR group and 11% (15/141) of the IMR group over 9 years of follow-up. Considering only the patients with recurrent moderate or severe MR, preoperative or late EF was less than 0.40 in 93% (14/15) of patients with IMR and 47% (14/30) of patients with NMR ($P = .007$). Three (2.1%) patients with IMR underwent late reoperation: 1 for ring dehiscence, 1 for inflammatory mitral stenosis, and 1 for chordal tethering from left ventricular aneurysm. No other patients had clinically apparent mitral stenosis. Twelve (3.0%) patients with NMR underwent late reoperation: 4 for endocarditis (occurrence rate of 0.2%/patient-year), 1 for hypertrophic outflow tract obstruction, 2 for late rupture of native chords, 1 for late rupture of polytetrafluoroethylene artificial chords, 1 for pannus ingrowth, 2 for heart transplantation for cardiomyopathy, and 1 for papillary muscle elongation.

A total of 93 deaths occurred over the 9 years of follow-up. Unadjusted 5-year mortality was worse for IMR (44% vs 16%, $P < .001$; Figure 1, A). In the univariable Cox model IMR was a significant predictor of long-term mortality, as were advanced age, most preoperative comorbidities, lower EF, higher NYHA class, CD, and reoperation (Table 2). However, in the full multivariable Cox model, only the number of preoperative comorbidities and advanced age were significant independent predictors of sur-

TABLE 2. Univariable Cox model predictors of survival

Variable	χ^2	P value	Hazard ratio	HR $\pm$ 95% CL
Age	23.60	<.0001	1.04	1.02-1.06
Female sex	0.00	.93	1.02	0.68-1.53
Hypertension	3.18	.07	1.48	0.96-2.26
Smoking	0.10	.75	0.90	0.48-1.70
Diabetes	17.30	<.0001	2.73	1.76-4.24
Renal	27.60	<.0001	4.14	2.60-6.60
Lung	15.90	<.0001	2.82	1.77-4.49
Peripheral vascular	7.53	.006	2.51	1.30-4.83
Cerebrovascular	4.37	.037	2.09	1.05-4.17
EF	20.20	<.0001	0.96	0.95-0.98
NYHA class	15.20	.0005	1.77	1.28-2.43
CD	24.80	<.0001	2.85	1.87-4.37
Prior operation	3.35	.05	1.79	1.00-3.22
Year of operation	0.00	.97	1.00	0.90-1.11
IMR	30.80	<.0001	3.22	2.14-4.84
Institution	0.05	.83	1.05	0.66-1.69

Results of univariable Cox model analysis are shown. Age was tested by 5-year increments. *HR*, Hazard ratio; *CL*, confidence limit; *EF*, ejection fraction; *NYHA*, New York Heart Association; *CD*, coronary disease; *Prior operation*, previous cardiac operation; *IMR*, ischemic mitral regurgitation versus nonischemic mitral regurgitation.

TABLE 3. Multivariable Cox model predictors of survival

Variable	χ^2	P value	Hazard ratio	HR $\pm$ 95% CL
No. of comorbidities	30.29	<.0001	1.62	1.37-1.93
Age	16.78	<.0001	1.29	1.14-1.46
Institution	1.50	.19	1.45	0.83-2.54
EF	1.43	.23	0.99	0.97-1.01
NYHA class	1.08	.30	1.21	0.85-1.73
IMR	0.97	.33	1.45	0.69-3.01
Female sex	0.69	.41	0.83	0.54-1.28
Prior operation	0.57	.45	1.27	0.69-2.34
CD	0.06	.81	0.91	0.43-1.93
Year of operation	0.00	.96	1.00	0.89-1.12

Results of multivariable Cox model analysis are shown. Age was tested by 5-year increments. *HR*, Hazard ratio; *CL*, confidence limit; *EF*, ejection fraction; *NYHA*, New York Heart Association; *IMR*, ischemic mitral regurgitation versus nonischemic mitral regurgitation; *Prior operation*, previous cardiac operation; *CD*, coronary disease.

vival ($P < .0001$). IMR, sex, EF, NYHA class, CD, prior operation, institution, and year of operation did not prove to be significant (all $P > .23$) (Table III).

When individual comorbidities were examined instead of the number of comorbidities, the only significant multivariable predictors of survival were advanced age, diabetes, renal disease, and lung disease (all $P < .012$), whereas IMR was not a predictor of survival ($P = .4$). By using propensity score analysis to stratify patients into 5 strata of high versus low propensity for IMR, IMR versus NMR also

Figure 2. Comparison of survival with IMR versus NMR by using stratification for propensity score. *Less than 10 patients in quintile.

failed to be a significant predictor either in the univariable or multivariable setting ($P = .1$, Figure 2).

Cox model analysis was repeated, examining only those patients with CD (Figure 3), and the raw unadjusted survival was worse for patients with IMR (5-year survival, $56\% \pm 5\%$ for patients with IMR versus $79\% \pm 7\%$ for patients with NMR; $P = .01$). However, by means of multivariable Cox modeling analysis, only age and number of comorbidities were significant independent predictors of survival (for patients with IMR, odds ratio = 1.7 (0.9-3.5); $P = .12$).

When survival of patients with IMR versus patients with NMR was adjusted for differences in the other 8 preoperative patient variables (age, sex, number of comorbidities, EF, NYHA class, CD, prior cardiac operation, and year of operation), long-term survival was not statistically different between the IMR and NMR group ($P = .33$; Figure 1, B). Specifically, the adjusted 5-year survival for patients with IMR (72%) closely approximated the 5-year survival for patients with NMR (80%). When CD and EF were combined in the model, their combined χ^2 value was 1.527 ($P = .466$), and comorbidities and age were still the only predictors of long-term mortality ($P < .0001$). When CD and EF were omitted (7-variable model), preoperative comorbidity and age were still the only predictors ($P < .0001$), and although the IMR variable contained more prognostic information ($\chi^2 = 3.133$), it still was statistically insignificant ($P = .077$).

Discussion

Most previous studies have compared long-term outcomes after surgical treatment of IMR versus NMR with univariable analyses. Bouchard and associates³ found that 5-year survival after mitral replacement was 70% for patients with IMR versus 80% for patients with NMR. In patients undergoing combined mitral and coronary surgery, Seipeli and coworkers²¹ demonstrated worse survival in patients with IMR than in patients with NMR (70% vs 85% at 5 years).

Figure 3. Survival of patients undergoing mitral valve repair with CD. IMR is compared with NMR (No IMR) before (A) and after (B) adjustment for differences in baseline patient characteristics.

Without direct comparison, Gillinov and associates^{2,7} reported 2 series from the same institution, with 5-year survival after mitral repair or replacement for IMR being 55% versus 76% for degenerative disease. In general, no prior study has attempted to differentiate IMR from other risk factors as independent determinants of postoperative outcome.

Previous hypotheses to explain the worse prognosis of IMR include more recurrent MR after repair of IMR,^{12,22} more significant underlying ventricular-subvalvular pathology, creation of mitral stenosis by undersized rings,⁹ increased comorbidity,²³ and a nebulous concept of ventricular remodeling.²⁴ The question addressed by this article is whether the adverse outcome after repair of IMR is due to unique differences in ischemic versus nonischemic cause or whether the higher mortality is simply a reflection of worse preoperative risk factors. The multivariable Cox model analysis suggests that the lower raw survival values after repair for IMR likely can be explained by higher preoperative risk factors alone, without impugning specific mitral or ventricular derangements.

Several technical factors might be important in producing less negative effect of IMR in the present series. First, rigid annuloplasty rings that fix mitral annular shape in addition to circumference were used in 95% of patients with IMR. Previous series have included patients receiving ringless repairs,¹² incomplete rings,²⁵ and flexible rings, all of whom might experience more recurrent MR.²⁴ It is now clear that reduction in the anterior to posterior mitral di-

mension is of critical importance in repair of IMR.²⁶ Not only will a rigid ring allow a larger valve area at a given anterior-posterior dimension, but fixing annular shape increases the surface area of leaflet coaptation (potentially compensating for early or late abnormalities in submitral geometry and providing an increased margin of safety). Undersizing the ring in patients with ventricular dilation or Carpentier type IIIb systolic leaflet restriction-tethering will have a similar effect of reducing mitral anterior-posterior annular diameter.⁹ Recurrent MR and reoperation rates in the present study were low and approximated those observed for NMR, emphasizing the effectiveness of rigid rings. On the basis of these data, one might hypothesize that routine rigid ring annuloplasty is the primary procedure of choice for moderate-to-severe IMR.

Also of importance are other considerations, such as reduced operative mortality caused by better postoperative pulmonary, renal, gastrointestinal, nutritional, antibiotic, and arrhythmia management. Reduction in acute mortality for repair of IMR to well under 10% in this and other series²⁷ might influence the risk factor analysis so that only preoperative comorbidity and age emerge as significant determinants of long-term outcome. Severe left ventricular dysfunction diminishes as a risk factor, perhaps because of maintenance of ventricular-valvular continuity²⁸ and optimization of early left ventricular function. Repair also provides the best chance for ventricular recovery from volume overload²⁹ in addition to reversal of ischemic dysfunction after CAB.³⁰ Just as interesting, CD does not seem to be a long-term risk factor, perhaps reflecting the beneficial effects of coronary revascularization.

This study has several limitations. First, one cannot exclude the possibility that IMR has some subtle negative effect on survival not detected in this relatively small sample of 535 patients.

Second, the observational nature of this study could have produced biases by not adequately accounting for inherent differences between the IMR and NMR groups and confounding institutional effects. Some inherent degree of collinearity of independent variables and inability to guarantee a complete list of independent variables are limitations of this and any retrospective analysis of complex and interrelated variables.

Third, the hypothesis tested might seem like a tautology in that IMR can be defined by using risk factors of EF and CD. In fact, however, this series included 20 patients with NMR with left ventricular dysfunction and CD, thus emphasizing that patients with IMR were only a subset of all patients with CD and impaired EF. Offsetting that limitation, when the analysis was performed without CD and EF, IMR remained an insignificant determinant of long-term survival relative to preoperative comorbidities and age.

Delayed or deferred referral of patients with IMR versus NMR for mitral repair purely on the basis of mitral disease cause is not supported by these data. Reluctance to refer patients with IMR for repair was evidenced in this study by the fact that patients with IMR with NYHA class I or II symptoms were rarely referred for surgical intervention (NYHA class I-II symptoms in 4% (5/141) of IMR referrals vs 23% (89/394) of NMR referrals, $P < .0001$). We strongly acknowledge that IMR and NMR are not the same; by definition, they are different. Here we present data that raise the concern that reluctance to refer patients with IMR for repair on the basis of the cause of valve damage alone is unwarranted and might deprive patients with IMR of potentially beneficial therapy.

In conclusion, with routine application of modern surgical techniques for mitral repair, IMR does not seem to be an independent predictor of long-term outcome after adjusting for age, preexisting comorbidities, and clinical findings. Future surgical risk assessment and therapeutic decision making should be based on overall patient condition and not be biased by ischemic cause of MR. It is notable that aggressive valve repair in IMR resulted in an adjusted survival that was similar to that in cases of NMR. Irrespective of whether this statistical result is unique to this series or can be reproduced in the future, it does indicate that outcomes have improved dramatically in the IMR subgroup with routine application of rigid ring annuloplasty.

References

1. Hickey MSJ, Smith LR, Muhlbaier LH, et al. Current prognosis of ischemic mitral regurgitation. *Circulation*. 1988;78(suppl I):151-9.
2. Salomon NW, Stinson EB, Griep RB, et al. Patient-related risk factors as predictors of results following isolated mitral valve replacement. *Ann Thorac Surg*. 1977;25:519-26.
3. Bouchard D, Pellerin M, Carrier M, et al. Results following valve replacement for ischemic mitral regurgitation. *Can J Cardiol*. 2001; 17:427-31.
4. Cohn LH, Rizzo RJ, Adams DH, et al. The effect of pathophysiology on the surgical treatment of ischemic mitral regurgitation: operative and late risks of repair versus replacement. *Eur J Cardiothorac Surg*. 1995;9:568-74.
5. Gillinov AM, Faber C, Houghtaling PL, et al. Repair versus replacement for degenerative mitral valve disease with coexisting ischemic heart disease. *J Thorac Cardiovasc Surg*. 2003;125:1350-62.
6. Mohty D, Orszulak TA, Schaff HV, et al. Very long-term survival and durability of mitral valve repair for mitral valve prolapse. *Circulation*. 2001;104(suppl I):111-17.
7. Gillinov AM, Wierup PN, Blackstone EH, et al. Is repair preferable to replacement for ischemic mitral regurgitation? *J Thorac Cardiovasc Surg*. 2001;122:1125-41.
8. Rankin JS, Livesey SA, Smith LR, et al. Trends in the surgical treatment of ischemic mitral regurgitation: effects of mitral valve repair on hospital mortality. *Semin Thorac Cardiovasc Surg*. 1989;1: 149-63.
9. Badhwar V, Bolling SF. Mitral valve surgery in the patient with left ventricular dysfunction. *Semin Thorac Cardiovasc Surg*. 2002;14: 133-6.
10. Morishita A, Shimakura T, Nonoyama M, et al. Mitral valve replacement in ischemic mitral regurgitation. Preservation of both anterior and posterior mitral leaflets. *J Cardiovasc Surg*. 2002;43:147-52.

11. Messas E, Guerrero JL, Handschumacher MD, et al. Chordal cutting: a new therapeutic approach for ischemic mitral regurgitation. *Circulation*. 2001;104(suppl 1):I958-63.
12. Czer LS, Maurer G, Bolger AF, et al. Revascularization alone or combined with suture annuloplasty for ischemic mitral regurgitation. Evaluation by color Doppler echocardiography. *Tex Heart Inst J*. 1996;123:270-8.
13. Dobre M, Koul B, Roger A. Anatomic and physiologic correction of the restricted posterior mitral leaflet motion in chronic ischemic mitral regurgitation. *J Thorac Cardiovasc Surg*. 2000;120:409-11.
14. Tibayan FA, Rodriguez F, Langer F, et al. Does septal-lateral annular cinching work for chronic ischemic mitral regurgitation? *J Thorac Cardiovasc Surg*. 2004;127:654-63.
15. Hvass U, Tapia M, Baron F, et al. Papillary muscle sling: a new functional approach to mitral repair in patients with ischemic left ventricular dysfunction and functional mitral regurgitation. *Ann Thorac Surg*. 2003;75:809-11.
16. Glower DD, Siegel LC, Frischmeyer KJ, et al. Predictors of outcome in a multicenter port-access valve registry. *Ann Thorac Surg*. 2000;70:1054-9.
17. Sheikh KH, Bengtson JR, Rankin JS, et al. Intraoperative transesophageal Doppler color flow imaging used to guide patient selection and operative treatment of ischemic mitral regurgitation. *Circulation*. 1991;84:594-604.
18. Johnson WD, Pedraza PM, Kayser KL. Preservation and restoration of the mitral mechanism during inferior wall aneurysmectomy. In: Duran CMG, Angell WW, Johnson AD, Oury JH, editors. Recent progress in mitral valve disease. London: Butterworth & Co; 1984.
19. David TE, Omran A, Armstrong S. Long-term results of mitral valve repair for myxomatous disease with and without chordal replacement with expanded PTFE. *J Thorac Cardiovasc Surg*. 1998;115:1279-86.
20. Rankin JS, Orozco RE, Rodgers TL, et al. Several new considerations in mitral valve repair. *J Heart Valve Dis*. 2004;13:399-409.
21. Seipeli RG, Schoendube FA, Yazquez-Jimenez JF. Combined mitral valve and coronary artery surgery: ischemic versus non-ischemic mitral valve disease. *Eur J Cardiothorac Surg*. 2001;20:270-5.
22. Tahta SA, Oury JH, Maxwell JM, et al. Outcome after mitral valve repair for functional ischemic mitral regurgitation. *J Heart Valve Dis*. 2002;11:11-8.
23. Grossi EA, Goldberg JD, LaPietra A, et al. Ischemic mitral valve reconstruction and replacement: comparison of long-term survival and complications. *J Thorac Cardiovasc Surg*. 2001;122:1107-24.
24. Miller DC. Ischemic mitral regurgitation redux—to repair to replace? *J Thorac Cardiovasc Surg*. 2001;122:1059-62.
25. Gorman JH, Gorman RC, Jackson BM, et al. Annuloplasty ring selection for chronic ischemic mitral regurgitation: lessons from the ovine model. *Ann Thorac Surg*. 2003;76:1556-63.
26. Tibayan FA, Rodriguez F, Langer F, et al. Annular remodeling in chronic ischemic mitral regurgitation: ring selection implications. *Ann Thorac Surg*. 2003;76:1549-55.
27. Adams DH, Filsoofi F, Aklog L. Surgical treatment of the ischemic mitral valve [abstract]. *J Heart Valve Dis*. 2002;11(suppl):S21-5.
28. Hansen DE, Cahill PD, Derby GC, et al. Relative contributions of the anterior and posterior mitral chordae tendineae to canine global left ventricular systolic function. *J Thorac Cardiovasc Surg*. 1987;93:45-52.
29. Bonchek LI, Olinger GN, Siegel R, et al. Left ventricular performance after mitral reconstruction for mitral regurgitation. *J Thorac Cardiovasc Surg*. 1984;88:122-7.
30. Rankin JS, Newman GE, Muhlbaier LH, et al. The effects of coronary revascularization on left ventricular function in ischemic heart disease. *J Thorac Cardiovasc Surg*. 1985;90:818-32.

Discussion

Dr David Adams (New York, NY). Don, congratulations to you and Scott and the coauthors of this study. Your observation that comorbidities are at least as important and perhaps even more important than the presence of IMR in determining survival in patients undergoing mitral repair might have important implications

for future guidelines regarding intervention in this complex patient population. I would like to emphasize that this is a unique study in that it represents one of the first and largest series of patients with moderate or severe IMR treated uniformly with downsized remodeling (ie, rigid or semirigid annuloplasty ring) with at least midterm follow-up. I have a few questions.

I wonder whether you could just clarify again recurrent MR in your study. When did it happen? How common was it?

Dr Glower. Again, we do not have complete information in that many of our patients came from a long distance away, and we do not have any echocardiographic follow-up data on them. Therefore, there is some potential bias there, but I think it is a fairly random bias. And in the 58% of patients in whom we did have echocardiographic data regarding recurrent regurgitation, as you saw in one graph, it tended not to recur immediately. It tended to recur either months or a few years out. And it is not surprising (but it was certainly statistically significant) that the patients who tended to get the recurrent regurgitation were those who had the lower EF preoperatively and especially those who were left with a low late EF. Not surprisingly, those are the ones who had late regurgitation.

Dr Adams. A few years ago Lishan Aklog presented the Brigham experience with mitral repair and IMR to this association, noting that patients with residual MR of greater than 2+ after repair had poorer survival compared with patients with lesser degrees of MR after repair. What was the significance of residual or recurrent MR in your study in terms of survival?

Dr Glower. That is a very good question. We actually have not looked at that yet to see whether there was association between late survival and those patients who did have late regurgitation. I suspect the answer would be that there is an association. This is because we know that those who had late regurgitation had lower EF, and certainly lower EF is associated with poorer survival. Therefore, I suspect the answer will be true, but we have not looked at that specifically.

Dr Adams. In your manuscript you noted a 7% operative mortality and a 4% 30-day mortality, which is quite good in the ischemic group, especially considering the study began in 1993 and 20% of your patients in the ischemic group were in fact undergoing reoperation. I wonder whether you can just tell us briefly about any strategies you have used to get those kinds of results?

Also, just comment on the inclusion of patients with single-vessel disease in this series. Do you think that biased the results in any way? Is it possible that any of these patients snuck in with degenerative disease, or, let's say, type 1 annular dilatation that was not related to pure ischemia because you included single-vessel disease?

Dr Glower. I think there is always the possibility of having some patients without an ischemic cause in here. But we went through these patients pretty carefully, and we pretty strictly followed the criterion of actually not only having impaired EF but also having a regional wall motion abnormality that was appropriate for the coronary lesion. Therefore, I think our series is pretty clean in that regard.

In terms of how many patients had single-vessel disease, it is not very many; I do not have the exact numbers. It is a relatively low number. A high percentage of these subjects had multivessel

coronary bypass grafting at the time. Certainly the results here are better than we are used to seeing in the literature. I think there are several factors here.

For one, this is clearly a more recent series than many of the series that are out there that extend back into an earlier era. We were fairly fortunate in being relatively early to downsize the ring in ischemic patients. I think many groups are coming to that realization only recently. I think we were just lucky to have done that at an earlier point in time, and I think that has been fairly important. Among other things, I think anesthesia obviously has improved, and there are even other more subtle things.

For example, there are a lot of redo patients in this series. In our hands the operative mortality for a redo sternotomy for IMR is at least 14% to 15%. In this series there were a significant number of patients who actually had a small port-access thoracotomy for isolated IMR, and we know from our own recent experience the mortality on that is probably only about 1%. Therefore, there are several things we know now and have incorporated into this series that probably have contributed to the mortality being lower than we might have traditionally thought for IMR.

Dr Adams. It is the biggest series I am aware of, with 24 and 26 rigid or semirigid rings, and therefore obviously this is a group that is worth continuing to follow. My last question is about EF and NYHA class. You did not find that either independently predicted survival in your study after mitral repair, which is in direct contrast to many studies in the literature. Can you clarify this for us further?

Dr Glower. That is a good question. Even though this is a relatively large series with more than 500 patients, we only had 90 deaths to look at statistically, and there are many factors that we would all suspect have to be predictors of mortality that did not come out as significant in this series, including EF and NYHA classification. I think part of that just might be a statistical power problem.

However, on the basis of earlier series, we would have expected that EF would have been much stronger, maybe one of the top 2 or 3 items, along with age or maybe redo operations, and it did not come out this way. And I can only speculate that perhaps the early and aggressive use of undersized rings might have protected us from some of that late mortality, if indeed the later deaths are related to recurrence.

Dr Bruce W. Lytle (Cleveland, Ohio). In your conclusion you implied that this is going to help you in terms of selection. I mean, if I could paraphrase the results of the study, what it shows is that if only these patients with ischemic heart disease or ischemic mitral insufficiency were not old, did not have comorbidities, and did not have coronary artery disease, they do really well, but they do, and so how has this helped you in terms of patient selection?

Dr Glower. I think it is more of a bias, perhaps more on the part of the cardiologists than on the part of surgeons, and I am sure that you see it also. There are quite a few patients out there with IMR of at least a moderate-to-severe degree who the cardiologist believes will never tolerate an operation. Whereas when a similar patient, 85 years old, might even have CD and mitral valve prolapse, they think this is obviously something they can repair and has much lower mortality. Therefore, the second patient gets referred. It is a fairly subtle concept, and it should not be too

surprising. Yet I think there really is a lot of thinking along that line that might be inappropriate.

Dr Richard J. Shemin (Boston, Mass). I think one of the unique aspects of this study is that more than 500 patients were operated on by only 2 surgeons; therefore, you get a lot of operative consistency. Can you share with us the surgeon's philosophy on downsizing? Do you always use the smallest ring on the shelf, or do you downsize 2 sizes? I think these technical aspects would be of interest. It is somewhat unusual to see the use of pledget-supported mattress sutures used in some of the valve repairs. I am interested in your indications and when you used pledget-supported sutures. Aggressive downsizing of a very larger annulus can lead to dehiscence of a ring. Did you experience this complication, resulting in a change in technique by using a pledget-supported mattress suture instead of the more common nonpledget-supported mattress suture technique?

Dr Glower. I think our series includes both pledget-supported sutures and nonpledget-supported sutures. I think you will find among persons here in the audience a pretty good mix of who does what. In my own practice I originally did not use pledget-supported sutures at all until I got 2 dehiscences, and I think it is important to look at those 2 patients with recurrent regurgitation.

One of them was someone who had a previous sternotomy, previous coronary bypass grafting. As best I could tell, he came to me with IMR and what I thought was about a 45-mm annulus, and I put a 26-mm ring in him. He did great for about a month, and then the ring dehiscence. Therefore, I took him back. I did a suture annuloplasty first. I put pledget-supported sutures in him, put a 26-mm ring back in, and he did fine. Therefore, what I have tended to do in the patients who have really massive dilation (particularly in a redo setting in which the redo mediastinum might pull the ventricle open) is to be a little bit more aggressive when placing pledget-supported sutures.

On the other hand, I do not do it routinely because sometimes I get a little bit more distortion of the valve leaflets with pledgets than otherwise. Therefore, I do not think there is a right or wrong there, unless you really have a lot of tension on a significantly dilated annulus. Then you should be aware and maybe think about pledget-supported sutures.

I think you are right that the consistency here with 2 surgeons and a relatively high volume might help a bit. We have had similar philosophies. Our sizing philosophy has been very simple. Obviously any patients who had prolapse or Barlow disease or big valves to begin with were not considered ischemic in this series. We put them in a nonischemic category, even though they might have had an infarction and even though they might have had dilation. Ischemic patients all had normal-sized valves. We would size the anterior leaflet and the distance between the commissures and then go down by 2 sizes. That pretty much routinely led us to 24 and 26 mm. We did not go to any fixed size. We would try to match it to the patient, and this is pretty much what we found.

Another question along those lines might be as follows: Is there something important about the fact that you chose complete rings or the fact that you chose rigid or semirigid rings? I do not know. We do not really have any data in our experience to compare complete with partial rings or rigid with semirigid rings to be able to answer that. I think the next article might be interesting in that

regard. Our decision was primarily based on the advice and thinking of Carpentier, who got us going on this.

There also are some data from Dr Miller recently leading us to think that there might be some advantages to maintaining the

septal-free wall distance, which a rigid ring might do better than a flexible ring. But we cannot really directly support that. We can just say that, taking the philosophy that we did take, the results were good and consistent.

Bound volumes available to subscribers

Bound volumes of *The Journal of Thoracic and Cardiovascular Surgery* are available to subscribers (only) for the 2005 issues from the Publisher, at a cost of \$134.00 for domestic, \$165.85 for Canadian, and \$155.00 for international subscribers for Vol 129 (January-June) and Vol 130 (July-December). Shipping charges are included. Each bound volume contains a subject and author index.

The binding is durable buckram with the Journal name, volume number, and year stamped in gold on the spine. Payment must accompany all orders. Contact Elsevier Inc., Subscription Customer Service, 6277 Sea Harbor Dr, Orlando, FL 32887, USA; phone 800-654-2452 or 407-345-4000.

Subscriptions must be in force to qualify. Bound volumes are not available in place of a regular Journal subscription.