Echocardiographic Prediction of Survival
After Surgical Correction of
Organic Mitral Regurgitation

Maurice Enriquez-Sarano, MD; A. Jamil Tajik, MD; Hartzell V. Schaff, MD; Thomas A. Orszulak, MD; Kent R. Bailey, PhD; Robert L. Frye, MD

Background Left ventricular dysfunction is a frequent cause of death after successful surgical repair of mitral regurgitation. The role of preoperative echocardiographic left ventricular variables in the prediction of postoperative survival and thus their clinical implications remain uncertain.

Methods and Results The survival of 409 patients operated on between 1980 and 1989 was analyzed. Of these, 253 (62%) were isolated mitral regurgitation and 135 (33%) had concomitant surgical procedures. The overall survival was 75% at 5 years (90% of expected), 58% at 10 years (88% of expected), and 44% at 12 years (73% of expected). Operative mortality was 6.6% and markedly improved from 1980 to 1984 (10.7%) to 1985 to 1989 (3.7%). Multivariate analysis showed that age (P = .0003), date of operation (P = .003), and functional class (P = .016) but not left ventricular function were predictors of operative mortality. In the most recent period (1985 to 1989), operative mortality was 12.3% in patients age 75 years or older and 1.1% in patients younger than 75 years. Late survival was analyzed in the operative survivors. Multivariate analysis showed that the most powerful predictor was echocardiographic ejection fraction (EF) (P = .0004), followed by age (P = .0031), creatinine level (P = .0062), systolic blood pressure (P = .0164), and presence of coronary artery disease (P = .0237). The late survival at 10 years was 32 ± 12% for EF < 50%, 53 ± 9% for EF 50% to 60%, and 72 ± 4% for EF ≥ 60%. The hazard ratio compared with EF ≥ 60% was 2.79 (95% confidence interval, 1.65 to 4.72) for EF < 50% and 1.81 (95% confidence interval, 1.11 to 2.95) for EF 50% to 60%. Echocardiographic EF remained the best predictor of late survival, even when combined with left ventricular angiographic variables. The survival of patients with EF ≥ 60% was 100% of expected at 10 years but was better in patients in class I or II than in those in class III or IV (82 ± 6% versus 59 ± 6%, respectively, at 10 years; P = .0021).

Conclusions In organic mitral regurgitation, (1) operative mortality has markedly decreased recently, being at a low 1.1% in patients younger than 75 years, and is predicted by age and symptoms and not by left ventricular function, and (2) left ventricular EF measured by echocardiography is the most powerful predictor of late survival. These results suggest that surgical treatment should be considered early, even in the absence of severe symptoms, in patients with severe mitral regurgitation, before left ventricular dysfunction occurs.

Key Words • ejection fraction • regurgitation • mitral valve

Mitral regurgitation is a valvular disease that produces complex hemodynamic alterations.1-4 However, severe regurgitation often produces minimal symptoms5 but still results in a high incidence of left ventricular dysfunction that might affect postoperative survival.6-7 The role of preoperative left ventricular function in predicting postoperative survival has been investigated in a limited number of clinical series that had conflicting results.8-13 In addition, the available data were obtained in patients with valve replacements performed mostly before 1980 and thus raise the question of their applicability to current practice.

Improvements in operative techniques and the use of repair procedures have decreased, albeit not eliminated, the risk of operation.14-17 However, the issues of the preoperative status of the patients and of the type of surgical correction should not be confused, and the ultimate decision on whether or not repair is technically feasible can only be made after inspection of the anatomic lesions by the surgeon. Therefore, the clinician’s decision on the timing of correction of mitral regurgitation can only be made on the basis of preoperative prognostic indicators. It is thus of clinical importance to identify preoperative markers of postoperative outcome independent of the type of surgical correction. We examined the outcome of patients operated on between 1980 and 1989 for organic mitral regurgitation and hypothesized that echocardiographic variables of left ventricular function (specifically ejection fraction and wall thickening) are important predictors of postoperative survival independent of the type of operation performed and should be incorporated into the clinical decision-making process.

Methods
This study was based on a retrospective review of our experience with surgical correction of mitral regurgitation.

The inclusion criteria were (1) surgical correction (repair or replacement) of mitral regurgitation performed between Jan-

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January 1, 1980, and December 31, 1989, (2) acquired, organic mitral regurgitation as defined by echocardiographic and surgical assessment, and (3) preoperative (within 6 months before operation) echocardiography allowing at least the measurement of the left ventricular ejection fraction. Patients with associated coronary artery bypass grafting were included.

The exclusion criteria were (1) previous operation for mitral regurgitation, (2) previous or associated aortic or tricuspid valve replacement (tricuspid valve repair was not excluded), and (3) patients with mitral regurgitation of ischemic or functional cause.

During that period, 2183 patients had mitral valve operation at our institution, 654 had isolated mitral regurgitation, and 409 met all inclusion and exclusion criteria.

Of the 409 patients representing our study population, mean age was 64±13 years, 163 were women and 246 were men, and 193 (47%) were in atrial fibrillation. The cause of mitral regurgitation was rheumatic in 42 patients, endocarditic in 40 patients, degenerative with valve prolapse in 311 patients, and miscellaneous in 16 patients. A ruptured chorda was present in 265 patients. The functional classification was New York Heart Association class I in 45 (11%), class II in 86 (21%), class III in 213 (52%), and class IV in 65 (16%). The surgical procedure performed was a valve repair in 195 patients and a valve replacement in 214. Coronary artery bypass grafting was performed in 99 patients.

Echocardiographic Analysis

Echocardiographic examination was performed at a mean of 23±31 days before surgery. The echocardiogram was analyzed at examination, as described previously.18 Throughout the study, the M-mode measurements were guided by two-dimensional echocardiography. The left ventricular diameters, ejection fraction,19,20 and wall thicknesses were measured, and the ratio of diameter to wall thickness was calculated at end diastole and end systole. Left atrial diameter was measured in systole. The end-systolic pressure was estimated21 from noninvasive blood pressure measurements, and the end-systolic wall stress was calculated as previously described.22 The end-systolic wall stress was normalized for the end-systolic volume index by using the angiographic value of this variable in 149 patients.

Coronary and Left Ventricular Angiography

Left ventricular quantitative angiography allowed calculation of the ejection fraction in 219 patients and left ventricular volumes in 201 patients. The correlation between echographic and angiographic ejection fraction (r=.61 overall, r=.70 in patients without coronary disease, SEE=9%) was acceptable for routine measurements. Coronary angiography was performed in 311 patients, among whom 119 presented with associated but unrelated coronary artery disease involving at least one vessel with stenosis ≥70%. Ninety-eight patients (52 men and 46 women) had no angina or history of myocardial infarction and did not have coronary angiography. Thus, coronary artery disease was classified as (1) proven associated coronary stenosis (n=119, 29%) and (2) absence of overt coronary artery disease (n=290, 71%).

Statistical Analysis

Group statistics were expressed as mean±1 SD. Group comparisons were performed with a standard t test or a χ2 test when appropriate. The cumulative probability of survival was estimated by the Kaplan-Meier method. The survival curves for the patients were compared with the expected survival of age- and sex-matched actuarial data from the 1980 United States white population and tested by using the one-sample log rank test. Unadjusted group survival comparison was based on the two-sample log rank test. The association of preoperative variables with overall and late survival was estimated with Cox proportional hazards models. Operative mortality was compared by the χ2 test for proportions and adjusted for baseline differences with a multivariate logistic analysis. Multivariate analyses were performed separately on clinical, echocardiographic, and angiographic variables and then in combination; the significant predictors then were included in a multivariate model incorporating the surgical type of correction (noted as repair or replacement) to confirm their independence from this variable. Because death is related to age in any population, the effect of preoperative variables on the age-adjusted excess mortality was analyzed by expressing the survival time of each patient in terms of the age- and sex-specific actuarial probability of dying at or before that time. This new age-adjusted survival time variable then was entered as the dependent variable in a multivariate Cox proportional hazards model analysis of survival. P<.05 was considered significant.

Results

The strategy of the analysis was to calculate survival and analyze predictors for (1) overall survival, (2) operative mortality, (3) late survival, and (4) age-adjusted survival. The preoperative echocardiographic characteristics of the population are summarized in Table 1.

Overall Survival

Follow-up evaluation was 98% complete up to the time of death or to 1992. At the latest follow-up, 122 patients were dead and 287 were alive. The overall survival was 75% at 5 years (90% of expected survival), 58% at 10 years (88% of expected survival), and 44% at 12 years (73% of expected survival), significantly lower than expected (P=.001) (Fig 1). The preoperative variables included as potential predictors of survival and results of multivariate analyses of survival are presented in Table 2. The combined multivariate analysis incorporating significant clinical and echocardiographic variables showed that the independent predictors of postoperative survival were preoperative echocardiographic

<table>
<thead>
<tr>
<th>Table 1. Preoperative Echocardiographic Characteristics of Patients With Organic Mitral Regurgitation</th>
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<tbody>
<tr>
<td><strong>Echocardiographic Variables</strong></td>
</tr>
<tr>
<td>EF, %</td>
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<tr>
<td>LVD, mm</td>
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<tr>
<td>LVS, mm</td>
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<tr>
<td>LA, mm</td>
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<tr>
<td>WT-D, mm</td>
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<tr>
<td>WT-S, mm</td>
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<tr>
<td>FWT, %</td>
</tr>
<tr>
<td>LVD-WT</td>
</tr>
<tr>
<td>LVS-WT</td>
</tr>
<tr>
<td>ESWS, 10⁵ dyne/cm²</td>
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<tr>
<td>ESWS/ESVI, 10⁵ dyne/cm² per mL per m²</td>
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</tbody>
</table>

EF indicates ejection fraction; ESWS, end-systolic wall stress; ESWS/ESVI, ratio of end-systolic wall stress to end-systolic volume index; FWT, wall thickening; LA, left atrial diameter; LVD, left ventricular end-diastolic diameter; LVD-WT and LVS-WT, ratio of left ventricular diameter to wall thickness in diastole and systole; LVS, left ventricular end-systolic diameter; and WT-D and WT-S, wall thickness in diastole and systole.
ejection fraction ($P=.0118$), age ($P<.0001$), creatinine level ($P=.0011$), presence of coronary artery disease ($P=.0007$), year of operation ($P=.0069$), and functional class ($P=.0186$). Atrial fibrillation was of borderline significance ($P=.0565$). The significance of these predictors was confirmed in a model including the type of surgical correction (repair or replacement). The combination of echocardiographic ejection fraction and angiographic end-systolic volume in a multivariate model showed that no additional survival information was provided by the angiographic variables.

### Operative Mortality

Twenty-seven patients (overall, 6.6%) died within 1 month of operation or during the same hospitalization. The cause of death in these 27 patients was myocardial infarction in 9, left ventricular failure in 3, prosthetic complications in 3 (hemorrhage, 2; embolism, 1), and procedural or noncardiac in 12 (rupture of left ventricle in 1, pulmonary embolism in 1, infection in 5, respiratory failure in 2, and multisystem failure in 3). The preoperative predictors of operative mortality are indicated in Table 2. Operative mortality could not be predicted from echocardiographic or angiographic variables, and only three clinical variables were independent predictors of operative mortality: age ($P=.0003$), year of operation ($P=.003$), and functional class ($P=.016$). Operative mortality was 18% (15 of 83) in patients older than age 75 years versus 3.7% (12 of 326) in patients younger than age 75 years. Operative mortality declined from 10.7% (18 of 168) during the 1980 to 1984 period to 3.7% (9 of 241) for the 1985 to 1989 period. The operative mortality was 9% (25 of 277) in classes III and IV versus 1.5% (2 of 132) in classes I and II. The effect of the combination of age and year of operation on the operative mortality is shown in Table 3. The younger patients (younger than age 75 years) operated on during the most recent period (1985 to 1989) had a low operative mortality—1.1% (2 of 184)—in this subset incorporating valve repairs (n=112) and valve replacements (n=72). Multivariate analysis including the type of correction (repair or replacement) confirmed the significance of the preoperative predictors of operative mortality independently of the type of correction.

### Late Mortality

Among the 382 operative survivors, 7 were lost to follow-up and 375 were included in the analysis of late mortality. Of the 375 patients, 95 died during late follow-up: of left ventricular dysfunction in 36 (intractable heart failure in 18 and sudden death in 18), valve-related complications in 25, complications of coronary artery disease in 14, noncardiac causes in 14, and unknown causes in 6. The clinical and echocardiographic predictors of late mortality are indicated in Table 3.

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**TABLE 2. Multivariate Analysis of Preoperative Variables Potentially Predicting Survival**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Overall Survival</th>
<th>Operative Survival</th>
<th>Late Survival</th>
</tr>
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<tbody>
<tr>
<td><strong>Clinical</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>.00001*</td>
<td>.0003*</td>
<td>.003*</td>
</tr>
<tr>
<td>Sex</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Year of operation</td>
<td>.0062*</td>
<td>.003*</td>
<td>NS</td>
</tr>
<tr>
<td>NYHA</td>
<td>.0024*</td>
<td>.016*</td>
<td>.016</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>.0271</td>
<td>NS</td>
<td>.013</td>
</tr>
<tr>
<td>CAD</td>
<td>.0009*</td>
<td>.08</td>
<td>.009*</td>
</tr>
<tr>
<td>Creatinine</td>
<td>.0001*</td>
<td>NS</td>
<td>.0005*</td>
</tr>
<tr>
<td>Systolic BP</td>
<td>NS</td>
<td>NS</td>
<td>.0205*</td>
</tr>
<tr>
<td><strong>Echocardiography</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>EF</td>
<td>.00001*</td>
<td>NS</td>
<td>.0009*</td>
</tr>
<tr>
<td>LVD</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
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<tr>
<td>LVS</td>
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<td>LA</td>
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<td>WT-D</td>
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<td>WT-S</td>
<td>NS</td>
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<td>FWT</td>
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<tr>
<td>LVD-WT</td>
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<td>NS</td>
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<tr>
<td>LVS-WT</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>ESWS</td>
<td>NS</td>
<td>NS</td>
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<tr>
<td>ESWS/ESVI</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
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<tr>
<td><strong>Angiography</strong></td>
<td></td>
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</tr>
<tr>
<td>EDVI</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>ESVI</td>
<td>.014</td>
<td>NS</td>
<td>.0027</td>
</tr>
<tr>
<td>EF</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>LV-end</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
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</tbody>
</table>

BP indicates blood pressure; CAD, coronary artery disease; EDVI, end-diastolic volume index; ESVI, end-systolic volume index; LV-end, left ventricular end-diastolic pressure; NYHA, New York Heart Association functional class; echocardiographic variables as in Table 1.

*Variable remaining significant in combined (clinical, echocardiography, angiography) multivariate analysis.

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**TABLE 3. Operative Mortality of Surgical Correction of Mitral Regurgitation**

<table>
<thead>
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<tbody>
<tr>
<td>Age, y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥75</td>
<td>31% (n=26)</td>
<td>12.3% (n=57)</td>
</tr>
<tr>
<td>&lt;75</td>
<td>7% (n=142)</td>
<td>1.1% (n=184)</td>
</tr>
</tbody>
</table>

Number of patients (in parentheses) indicate operative mortality in each subgroup.
The significance: functional graphic powerful predictor

FIG 2. Graph of late survival of operative survivors according to preoperative echocardiographic ejection fraction (EF). Number at risk for each interval is indicated at bottom.

Table 2. The combined multivariate analysis of clinical and echocardiographic variables showed that the most powerful predictor of late mortality was echocardiographic ejection fraction (P = .0004), followed by age (P = .0031), creatinine level (P = .0062), systolic blood pressure (P = .0164), and presence of coronary artery disease (P = .0237), with two other variables having borderline significance: functional class (P = .0524) and presence of atrial fibrillation (P = .0575). The late survival according to the level of ejection fraction (at 10 years, 32 ±12%, 53 ±9%, and 72 ±4%, respectively, for ejection fraction <50%, 50% to 60%, and ≥60%) is presented in Fig 2. The hazards ratio compared with ejection fraction ≥60% was 2.79 (95% confidence interval, 1.65 to 4.72) for ejection fraction <50% and 1.81 (95% confidence interval, 1.11 to 2.95) for ejection fraction 50% to 60%. The estimated 5-year survival and yearly mortality according to preoperative ejection fraction, symptoms, and presence of coronary artery disease are presented in Table 4. The combination of echocardiographic ejection fraction (globally or subdivided in calculated or estimated) and angiographic end-systolic volume in a single multivariate model showed that no additional survival information was provided by the angiographic variable.

To confirm the predictive value of echocardiographic ejection fraction independent of the type of operation performed, the late survival was compared in subgroups defined according to the level of ejection fraction and separately in patients with mitral valve repair and in patients with mitral valve replacement (Fig 3). The effect on survival of ejection fraction remained valid in both subsets of patients and was confirmed by the multivariate analysis incorporating the type of operation performed (repair, replacement, coronary artery bypass graft) with the multivariate model of survival analysis (P = .0011).

In the subset of patients with ejection fraction ≥60%, the survival was excellent, representing 100% of the expected survival at 10 years (Fig 4), but in patients with minimal symptoms (class I or II), survival was significantly better than in patients with severe symptoms (class III or IV): at 10 years, 82 ±6% versus 59 ±6% (P = .0021) (Fig 4).

Age-Adjusted Survival

Multivariate analysis of age-adjusted survival showed that (1) overall, age was not associated with long-term excess mortality. This absence of global effect was the result of the previously demonstrated excess operative mortality and a decreased late age-adjusted hazard. This combination is clearly demonstrated by the survival curves of patients older and younger than age 75 years, representing at 9 years in both groups 87% of their corresponding expected survival, as shown in Fig 5. (2) Echocardiographic ejection fraction remained the most powerful predictor of late age-adjusted survival (P = .0009).

Discussion

This consecutive series of 409 patients with organic mitral regurgitation operated on between 1980 and 1989 shows that operative mortality, which was 6.6% overall, (1) was markedly improved in the last 5 years of this experience, to 3.7%, (2) was unrelated to the variables of left ventricular function, and (3) was mainly related to symptoms and to age, being at a low 1.1% in patients younger than age 75 years in the most recent experience.

Long-term survival, which was 58% at 10 years (88% of predicted), was related (1) mainly to the preoperative echocardiographic ejection fraction and (2) also to clinical factors such as systolic blood pressure, creatinine level, and presence of coronary artery disease, with a borderline effect of atrial fibrillation and preoperative symptoms.

These predictors of short- and long-term postoperative survival are valid whether the surgeon can perform a repair or has to replace the mitral valve.

These results confirm the decline in operative mortality observed recently14,23,24 and in series16,17,25,26 incorporating a significant number of valve repairs. Despite these improved results, the risk of operation has not been eradicated and the clinical decision-making process remains individualized, based on preoperative predictors of outcome. Unfortunately, the risk of the surgical procedures has been globally described,16,17,27-33 but in patients with mitral regurgitation, despite a worse survival than in mitral stenosis,27,34 the specific preoperative predictors of outcome remain ill-defined.

Risk factors of operative mortality have not been uniform: functional class, a recent myocardial infarction, and hepatic dysfunction26; age, functional class, papillary muscle scarring, and left ventricular resection for aneurysm36; or coronary artery disease13,33 were significant predictors of operative mortality. For late survival, the information specifically pertaining to mitral regurgitation is limited, and the predictors included age,12,35 pulmonary rales,10 left atrial size,10 various

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Table 4. Predicted 5-Year Survival of Operative Survivors

<table>
<thead>
<tr>
<th>Variable</th>
<th>Ejection Fraction</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>≥60%</td>
</tr>
<tr>
<td>No risk factor</td>
<td>93 (1.44)*</td>
</tr>
<tr>
<td>Class III-IV, no CAD</td>
<td>87 (2.81)</td>
</tr>
<tr>
<td>Class I-II and CAD</td>
<td>87 (2.86)</td>
</tr>
<tr>
<td>Class III-IV and CAD</td>
<td>75 (5.52)</td>
</tr>
</tbody>
</table>

CAD indicates coronary artery disease.

*Numbers indicate, in patients surviving the operative period, probability of 5-year survival as a percentage and yearly mortality (in parentheses).
preoperative indices of left ventricular function, postoperative variables of left ventricular function, and presence of coronary disease. However, these studies included mostly patients operated on before 1980, some with ischemic mitral regurgitation, and the number of patients with valve repair was limited. Consequently, it is essential to determine the preoperative predictors of survival in a series of patients with pure mitral regurgitation of organic cause, operated on recently, taking into account the recent progress in operative care and procedures.

**Left Ventricular Function and Prediction of Survival After Correction of Mitral Regurgitation**

Mitral regurgitation induces a change in the loading condition of the left ventricle that could affect the indices of left ventricular function. The regurgitant volume may influence the left ventricular function by increasing the left ventricular end-diastolic volume, and the correction of the ejection fraction by preload has been suggested. The changes in afterload are more complex, and the decreased impedance to ejection is at variance with the end-systolic wall stress, which reflects afterload and has been found within the normal range in patients with mitral regurgitation. With increasing end-systolic wall stress, ejection fraction decreases. The volume-corrected end-systolic wall stress and the slope of the end-systolic pressure-volume relation (Emn) have been suggested as indices sensitive to subtle changes in left ventricular function in patients with mitral regurgitation.

Even though some theoretical issues are incompletely resolved in the assessment of left ventricular function, for clinical purposes it is of utmost importance to determine in patients with mitral regurgitation the predictive value for postoperative survival of simple measures of left ventricular function obtained by techniques applicable to a large number of patients in order to improve the clinical decision-making process.

Although the literature suggests that preoperative left ventricular indices may affect postoperative survival, the analysis has not always been focused on pure, isolated, organic mitral regurgitation, and no consensus has been reached.

Some reports have shown conflicting results regarding the relation between left ventricular function and early mortality. However, in the present study, no echocardiographic examination included the assessment of left ventricular function.
The role of left ventricular function indices as predictors of late survival has been even more elusive. (1) The predictors found were nonuniform: left ventricular end-diastolic pressure, \textsuperscript{27} ejection fraction, \textsuperscript{6,11} end-systolic radius to wall thickness ratio, \textsuperscript{10} and end-systolic wall stress to volume index ratio. In addition, these series included only valve replacements, \textsuperscript{8-13} small numbers of patients, \textsuperscript{8,11,12} mixed valve disease, \textsuperscript{11} reoperations, \textsuperscript{10} and associated valve lesions, \textsuperscript{10} limiting their impact. (2) Moreover, different indices were described as predictors of related end points such as functional status\textsuperscript{59-61} or postoperative left ventricular function.\textsuperscript{42-44} (3) The role of echocardiographic assessment of left ventricular function remains uncertain.\textsuperscript{10}

In the present series, preoperative echocardiographic left ventricular ejection fraction was the only independent ventricular variable as well as the most powerful predictor of late survival. Despite the potential influence of loading conditions on ejection fraction, its clinical usefulness is clearly demonstrated by its strong prognostic power. The important predictive value of preoperative ejection fraction on late survival is consistent with some older series\textsuperscript{9,11,45} and confirms studies\textsuperscript{6,7,46} that showed that preoperative ejection fraction is the strongest predictor of postoperative left ventricular function. It also underlines the role of left ventricular dysfunction as the major cause of late death after operation for mitral regurgitation.\textsuperscript{5,7,47,48} The predictive value of preoperative echocardiographic ejection fraction is not increased by angiographic variables and is valid whether repair or replacement is performed. Valve repair, which is a major advance in mitral regurgitation surgery,\textsuperscript{15,56,49} potentially influences the postoperative left ventricular function by maintaining the normal subvalvular apparatus.\textsuperscript{51,50-52} However, it does not eliminate the risk of postoperative left ventricular dysfunction\textsuperscript{6,51} and the predictive value of preoperative ejection fraction for survival.

In patients with ejection fraction \( \geq 60\% \), there is no excess late mortality compared with the reference population. Nevertheless, in the same subset with ejection fraction \( \geq 60\% \), the patients with class III or IV symptoms have a significantly worse overall survival than the minimally symptomatic patients (class I or II).

**Other Predictors of Survival**

**Age**

Age is a predictor of survival, even in the absence of any detected disease. Even though age has been considered as a predictor of survival in patients with mitral regurgitation,\textsuperscript{12,26,35} the potential of advanced age for inducing excess mortality is difficult to document. In the present series, age is a predictor of survival but not of long-term excess mortality compared with expected mortality (Fig 3). However, advanced age is a strong factor in operative mortality,\textsuperscript{24,26,27,31} and this excess operative mortality is still of clinically significant magnitude and cannot be ignored in clinical decision making.

**Functional Class**

Functional class is an independent predictor of early mortality\textsuperscript{23,26,27,29} and was of borderline significance as a predictor of late mortality. These results confirm previous observations and show that, for any given age and ejection fraction, the option of waiting for severe symptoms before proceeding with surgical correction of mitral regurgitation is associated with a significant postoperative excess mortality.

**Coronary Artery Disease**

Coronary artery disease is of borderline significance as a predictor of operative mortality and an independent predictor of late mortality, in agreement with previous reports.\textsuperscript{13,26,27,33} However, the natural history of patients with severe organic mitral regurgitation and coronary artery disease and the potential effect of coronary artery bypass grafting on the prognosis deserve further study.

**Creatinine Level and Systolic Blood Pressure**

These are also independent predictors of late but not operative survival, probably corresponding to more diffuse or severe vascular disease, which is not surprising in this age group\textsuperscript{53,54} and probably unrelated to the mitral valve disease.

**Clinical Implications**

The incidence of left ventricular dysfunction as a cause of late death is, in our opinion, too high and should be prevented by surgical correction of mitral regurgitation at an earlier date. The progressive decline in operative mortality and the advances in valve repair make these early surgical indications more attractive. Age, symptoms, and left ventricular ejection fraction should be the three main variables taken into account in the surgical decision. Patients in classes III and IV should continue to be evaluated for immediate operation.

In patients age 75 years or older, even though operative mortality has decreased, it is still significant, and the surgical indication should continue to be made on the basis of the symptoms. This approach could be revised if further improvements in operative mortality are observed.

In patients younger than age 75 years, the current operative mortality is extremely low and allows consideration of operation in patients with no or minimal symptoms (class I or II). In patients with an ejection fraction...
<50%, the late mortality is high, but operation should not be contraindicated and has been shown to improve survival.\textsuperscript{35,55} In patients with an ejection fraction of 50% to 60%, there is an increased risk of postoperative left ventricular dysfunction and excess mortality, and surgical treatment probably should not be delayed. In patients with an ejection fraction $\geq 60\%$, the surgical outcome is usually excellent but better without than with severe symptoms. Thus, for patients in class I or II, operation may certainly be considered on an individual basis, especially in those with the most severe regurgitation and if the lesions appear repairable. This early indication with no or mild symptoms and no sign of left ventricular deterioration emphasizes the role of quantitative assessment of severity of mitral regurgitation (now available noninvasively\textsuperscript{56,57}) to confirm the degree of regurgitation before exposing patients to a surgical risk, even for a valve repair.

Limitations of the Study

The use of echocardiographic left ventricular measurements may be a concern. However, two-dimensional echocardiography was used to direct all the measurements. Moreover, the measurement of ejection fraction as it was performed in our study has not only been validated\textsuperscript{19,20} but its high reproducibility\textsuperscript{58} and the value of its echocardiographic estimation\textsuperscript{59,60} have been confirmed. Also, echocardiography was superior to left ventricular angiography for the prediction of postoperative survival, demonstrating that echocardiographic measurements do not represent a limitation.

Left ventricular elastance and stiffness\textsuperscript{38} were not measured in this study. These measurements are important tools, but their additional value in predicting survival after surgical correction of mitral regurgitation remains to be determined.

The influence of the type of surgical correction performed on postoperative survival is an important issue, but it should not be confused with the preoperative status of the patients for the following reasons. (1) The potential beneficial impact of valve repair on survival is controversial\textsuperscript{26,49} and has been analyzed separately.\textsuperscript{61} (2) The current study demonstrates that left ventricular dysfunction is associated with excess late mortality even in patients who have a valve repair. (3) Preoperative variables remained independent predictors of survival in a combined model incorporating the type of correction performed. Thus, the preoperative status of patients, in particular the echocardiographic assessment of left ventricular function, should always be incorporated in the clinical decision making.

Conclusions

The present study of 409 patients operated on for isolated, pure, organic mitral regurgitation showed that (1) the operative mortality, overall of 6.6%, has decreased in the most recent period to 3.7% and to a low 1.1% in patients younger than age 75 years and is mainly predicted by age and symptoms at operation but not by left ventricular function, and (2) the left ventricular ejection fraction measured by echocardiography is the most powerful preoperative predictor of late survival. To decrease the late mortality due to left ventricular dysfunction, earlier surgical treatment in patients with severe mitral regurgitation should be considered before left ventricular function deterioration.

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