Is there an outcome penalty linked to guideline-based indications for valvular surgery? Early and long-term analysis of patients with organic mitral regurgitation

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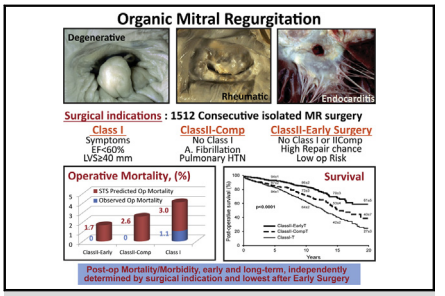
ABSTRACT

Objective: The timing of surgical correction of mitral regurgitation remains controversial. A major source of dispute regards the potential short- and long-term postoperative outcome penalty associated with the type of guideline-based indication for surgery.

Methods: Between 1990 and 2000, 1512 patients (aged 64 ± 14 years, mitral prolapse in 89%, valve repair in 88%) underwent surgical correction of pure organic mitral regurgitation. Patients were stratified according to surgical indication into class I triggers (ClassI-T: heart failure symptoms, ejection fraction <60%, end-systolic diameter ≥40 mm, n = 794), class II triggers based on clinical complications (ClassII-CompT: atrial fibrillation or pulmonary hypertension, n = 195), or early class II triggers based on a combination of severe mitral regurgitation and high probability of valve repair (ClassII-EarlyT: n = 523).

Results: Operative mortality was highest with ClassI-T (1.1% vs 0% and 0%, $P = .016$). Long-term survival was lower with ClassI-T (15-year 42% ± 2%; adjusted hazard ratio [HR], 1.89; 95% confidence interval [CI], 1.53-2.34; $P < .0001$) and ClassII-CompT (15-year 53% ± 4%, adjusted HR, 1.39; 95% CI, 1.04-1.84; $P = .027$) versus ClassII-EarlyT (15-year 70% ± 3%, $P < .0001$). Postoperative excess mortality with ClassI-T and ClassII-CompT was confirmed by age stratification, inverse probability weighting, and expected survival adjustment. Excess postoperative heart failure was high with ClassI-T (adjusted HR, 2.49; 95% CI, 1.82-3.47; $P < .0001$) and ClassII-CompT (adjusted HR, 1.98; 95% CI, 1.30-3.00; $P = .002$).

Conclusions: The type of guideline-based indication for surgical correction of organic mitral regurgitation is associated with profound outcome consequences on long-term postoperative mortality and heart failure, despite low operative risk and high repair rates. Conversely, surgical correction of severe mitral regurgitation based on high probability of repair (ClassII-EarlyT) is associated with improved survival and low heart failure risk and should be the preferred strategy in valve centers offering low operative risk and high repair rates. (J Thorac Cardiovasc Surg 2015;150:50-8)



From *top* to *bottom*: lesions of organic MR, classes of indications, and outcomes by indication.

Central Message

Guideline triggers for MR surgery based on symptoms and complications are linked to excess postoperative mortality/morbidity versus early surgery. Early repair should be preferred to rescue surgery in patients with MR.

Perspective

Controversy regarding the timing of surgery for organic MR hinges on the assumption that guideline-based triggers allow safe outcomes. Surgical improvements, higher repair rates, and lower operative mortality may support this assumption. In 1512 patients undergoing operation for organic MR (repair 88%, operative mortality 0.6%), triggers for class I (symptoms, EF <60%, end-systolic diameter ≥40 mm) were independently associated with doubling of long-term death/heart failure risk, and triggers for class II (atrial fibrillation, pulmonary hypertension) were associated with a 40% increase in risk. Thus, these triggers lead to rescue surgery when present initially, but this is not the preferred surgical timing. Early surgery, performed in centers with high repair rates and low risk, with outstanding outcomes should be the preferred strategy.

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Abbreviations and Acronyms
CABG = coronary artery bypass grafting
CHF = congestive heart failure
CI = confidence interval
EF = ejection fraction
HR = hazard ratio
IPW = inverse probability weight
LV = left ventricular
MR = mitral regurgitation
STS = Society of Thoracic Surgeons

Guidelines for the clinical management of organic mitral regurgitation (MR) are similar between US[1] and European[2] versions. These guidelines define the triggers for surgical indications; class I triggers (heart failure symptoms, low left ventricular [LV] ejection fraction [EF], or large end-systolic dimension) generally mandate prompt operation, whereas class II triggers, whether guided by clinical complications (atrial fibrillation, pulmonary hypertension) or high MR severity and repairability (early surgery), are less rigid with leeway for clinical judgment.[1,2] Although the guidelines vary little between versions, they are based on level C evidence, that is, mainly expert opinions. Thus, an intense debate persists regarding the best timing for MR surgery.[3,4]

Class I triggers for MR surgery are based on studies of the 1990s analyzing outcomes of patients who underwent surgery in the 1980s.[5-7] Symptoms,[6,8] decreased EF,[5,9] or large LV end-systolic diameter[10] were all mentioned as affecting postoperative outcome, suggesting a penalty related to these triggers. Likewise, class II triggers considered as "minor" complications may have long-term consequences.[11,12] However, improvements have occurred since these pilot studies; there has been a decline in operative mortality and a marked increase in performance of valve repair,[13] which may protect against the postoperative consequences of these triggers.[14] Thus, whether long-term surgical outcome, in the era of valve repair and low operative risk, is similar irrespective of surgical triggers or is affected by triggers indicating MR surgery is unclear and may be crucial to formulate clinical guidelines. Thus, it is essential to analyze long-term outcome according to the triggers that led to surgery. To address this conundrum, new data are warranted, and we analyzed consecutive patients undergoing operation for organic MR between 1990 and 2000 to obtain a sufficiently long follow-up. We examined the null hypothesis that indications for organic MR surgery were not independently associated with differences in clinical outcome, particularly long-term survival.

MATERIALS AND METHODS

Subjects

Eligible patients were those who underwent mitral surgery at the Mayo Clinic (Rochester, Minn) for pure isolated organic (surgically verified intrinsic structural mitral disease) MR between January 1, 1990, and December 31, 2000. We excluded patients associated mitral stenosis, concomitant aortic valve replacement/repair or tricuspid valve replacement, previous valve replacement/repair or congenital heart disease surgery, or with pericardial, myocardial intrinsic disease or ischemic MR with or without papillary muscle rupture. The study was approved by the Mayo Clinic Institutional Review board as a low-risk study.

Baseline Characteristics

Clinical symptoms of recent murmur (<6 months), comorbidity, blood pressure, and heart rate were noted as classic MR signs. Electrocardiogram allowed the diagnosis of atrial fibrillation. Doppler echocardiography measured LV diameters and EF, quantified MR and pulmonary pressure, and determined MR cause, mechanisms, and associated cardiac conditions.[15] Catheterization diagnosed obstructive coronary disease (>50% left main, >70% other segments). With the entire information available, a risk score was calculated using the Society of Thoracic Surgeons (STS) algorithm based on the coefficient provided by the Society in 2013.[16] Indication for surgery relied on shared decision-making by the patient, cardiologist, and cardiac surgeon. We classified surgical indications by guideline-based preoperative characteristics as class I (heart failure symptoms, EF <60%, or end-systolic LV diameter ≥40 mm; ClassI-T group) and as class II due to clinical "minor" complication (no ClassI-T but with atrial fibrillation or pulmonary hypertension systolic pulmonary pressure ≥50 mm Hg; ClassII-CompT group). Patients with severe MR, no other surgical trigger, and undergoing early surgery with a high probability of valve repair comprised the ClassII-EarlyT group.

Operative Characteristics

Operative reports verified anatomic mitral lesions. Surgery performed (repair vs replacement), concomitant coronary artery bypass grafting (CABG), and duration of cardiopulmonary bypass were recorded. Residual MR after resumption of normal circulation (by transesophageal echocardiography or double-sampling dye curves) was systematically noted. Postoperative complications recorded were perioperative mortality (within 30 days of surgery or same hospitalization), need for circulatory support beyond the first postoperative day, intra-aortic balloon pump, low cardiac output syndrome postoperatively, and renal failure postoperatively. Finally, the total number of days spent in the hospital was counted.

Long-Term Clinical Outcome

Follow-up after discharge was obtained through clinical visits at our institution or affiliated clinics and hospitals and through questionnaires to patients. Data were collected throughout the follow-up period to detect transient events. Additional information was obtained using communication with personal physicians, patients, and next of kin, or use of death or autopsy certificates. Thus, we obtained follow-up until death or at least 10 years postoperatively in 92% of patients. The main end point was long-term postoperative survival as a simple categoric measure of outcome. Secondary end points were postoperative occurrence of heart failure defined using Framingham signs and symptoms criteria[17] as cardiac-specific measures of outcome and occurrence of the combined end point of death or heart failure.

Statistical Analysis

Baseline characteristics are described as mean ± standard deviation for continuous variables and percentages for categoric variables. Comparisons between groups were made using analysis of variance with Tukey post hoc testing for continuous variables and chi-square or Fisher exact test as necessary for categoric variables. Long-term survival and event rates were summarized using the Kaplan–Meier method for estimating