

ORIGINAL ARTICLE

Mitral-Valve Repair versus Replacement for Severe Ischemic Mitral Regurgitation

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ABSTRACT

BACKGROUND

Ischemic mitral regurgitation is associated with a substantial risk of death. Practice guidelines recommend surgery for patients with a severe form of this condition but acknowledge that the supporting evidence for repair or replacement is limited.

METHODS

We randomly assigned 251 patients with severe ischemic mitral regurgitation to undergo either mitral-valve repair or chordal-sparing replacement in order to evaluate efficacy and safety. The primary end point was the left ventricular end-systolic volume index (LVESVI) at 12 months, as assessed with the use of a Wilcoxon rank-sum test in which deaths were categorized below the lowest LVESVI rank.

RESULTS

At 12 months, the mean LVESVI among surviving patients was 54.6 ± 25.0 ml per square meter of body-surface area in the repair group and 60.7 ± 31.5 ml per square meter in the replacement group (mean change from baseline, -6.6 and -6.8 ml per square meter, respectively). The rate of death was 14.3% in the repair group and 17.6% in the replacement group (hazard ratio with repair, 0.79; 95% confidence interval, 0.42 to 1.47; $P=0.45$ by the log-rank test). There was no significant between-group difference in LVESVI after adjustment for death (z score, 1.33; $P=0.18$). The rate of moderate or severe recurrence of mitral regurgitation at 12 months was higher in the repair group than in the replacement group (32.6% vs. 2.3%, $P<0.001$). There were no significant between-group differences in the rate of a composite of major adverse cardiac or cerebrovascular events, in functional status, or in quality of life at 12 months.

CONCLUSIONS

We observed no significant difference in left ventricular reverse remodeling or survival at 12 months between patients who underwent mitral-valve repair and those who underwent mitral-valve replacement. Replacement provided a more durable correction of mitral regurgitation, but there was no significant between-group difference in clinical outcomes. (Funded by the National Institutes of Health and the Canadian Institutes of Health; ClinicalTrials.gov number, NCT00807040.)

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FUNCTIONAL ISCHEMIC MITRAL REGURGITATION affects 1.6 million to 2.8 million patients in the United States and is associated with a doubling in mortality among patients with mild or greater degrees of mitral regurgitation after myocardial infarction.¹⁻³ Ischemic mitral regurgitation is a consequence of adverse left ventricular remodeling after myocardial injury with enlargement of the left ventricular chamber and mitral annulus, apical and lateral migration of the papillary muscles, leaflet tethering, and reduced closing forces. These processes lead to malcoaptation of the leaflets and variable degrees of mitral regurgitation that can fluctuate dynamically as a function of volume status, afterload, heart rhythm, and residual ischemia. The leaflets themselves are normal, and the disease occurs in the myocardium rather than in the valve itself. As such, the treatment of functional ischemic mitral regurgitation differs considerably from that of primary, degenerative mitral regurgitation.⁴

Practice guidelines recommend consideration of mitral-valve repair or chordal-sparing replacement for patients with severe ischemic mitral regurgitation that is causing limiting symptoms despite the best available medical therapy and, possibly, cardiac resynchronization.^{5,6} These guidelines, however, do not specify whether to repair or replace the mitral valve, because conclusive evidence is lacking to indicate which of these interventions is superior. Clinical studies have suggested that repair is associated with lower perioperative mortality,⁷⁻¹⁰ whereas replacement provides better long-term correction with a lower risk of recurrence (an important consideration, since recurrence of mitral regurgitation confers a predisposition to heart failure, atrial fibrillation, and readmission). This perceived tradeoff between reduced operative morbidity and mortality with repair and better long-term correction of ischemic mitral regurgitation with replacement has generated substantial variation in surgical practice for this high-prevalence condition.⁴

The Cardiothoracic Surgical Trials Network (CTSN) conducted a multicenter, randomized trial to evaluate the relative benefits and risks of repair versus replacement, with or without coronary revascularization, in patients with severe ischemic mitral regurgitation.

METHODS

STUDY DESIGN AND OVERSIGHT

We randomly assigned patients with chronic, severe ischemic mitral regurgitation, in a 1:1 ratio, to undergo either mitral-valve repair or chordal-sparing replacement. The randomization was stratified according to center and blocked to ensure ongoing equivalence of group size. The trial was designed to enroll 250 patients; 1 additional patient underwent randomization before the completion of enrollment. Investigators were unaware of overall outcome data. End points were measured at 30 days and at 6, 12, and 24 months; the 24-month follow-up is ongoing.

The trial was conducted at 22 clinical centers, with a coordinating center, an independent committee that adjudicated causes of death and adverse events, and a data and safety monitoring board, appointed by the National Institutes of Health, that oversaw trial progress. The institutional review board at each study center approved the protocol, which is available with the full text of this article at NEJM.org. All patients provided written informed consent.

PATIENTS

The target population was adults with severe ischemic mitral regurgitation and coronary artery disease who were eligible for surgical repair or replacement of their mitral valves, with or without coronary-artery bypass grafting (CABG). Severe ischemic mitral regurgitation was assessed by means of resting transthoracic echocardiography on the basis of integrative criteria¹¹ that were verified by an independent core laboratory. Severe mitral regurgitation was defined as an effective regurgitant orifice area of 0.4 cm² or more. If the effective regurgitant orifice area was less than 0.4 cm², the assessment of the severity of mitral regurgitation was guided by associated findings, including the ratio of the jet area to the left atrial area, the width of the vena contracta, the density of the continuous-wave Doppler profile of mitral systolic function, the pulmonary-vein systolic flow pattern, and left-sided chamber dimensions.

Exclusion criteria included any echocardiographic evidence of structural (chordal or leaflet) mitral-valve disease or ruptured papillary

muscle. Complete eligibility criteria have been reported previously.¹²

INTERVENTIONS

Mitral-valve replacement included complete preservation of the subvalvular apparatus. The technique of preservation, type of prosthetic valve, and technique of suture placement were chosen according to the preference of the surgeon, as was the type of annuloplasty ring in the repair group. The protocol mandated the use of an approved rigid or semirigid complete annuloplasty ring, which was downsized for the annulus diameter. All patients were to receive guideline-directed medical therapy by their treating cardiologist, including aspirin, lipid-lowering agents, beta-blockers, and angiotensin-converting-enzyme inhibitors, as well as cardiac-resynchronization therapy.

END POINTS

The primary end point of the trial was the degree of left ventricular reverse remodeling, as assessed by means of the left ventricular end-systolic volume index (LVESVI) on the basis of transthoracic echocardiography performed 12 months after randomization. The LVESVI was verified by the echocardiography core laboratory. Secondary end points included mortality, a composite of major adverse cardiac or cerebrovascular events (rate of death, stroke, subsequent mitral-valve surgery, hospitalization for heart failure, or an increase in New York Heart Association [NYHA] class of ≥ 1), serious adverse events, recurrent mitral regurgitation, quality of life, and rehospitalization.

STATISTICAL ANALYSIS

The trial was designed with a power of 90% to detect a between-group difference of 15 ml per square meter in the LVESVI from baseline to 12 months. We assumed a baseline LVESVI of 100 ml per square meter, improvements of 20 ml per square meter in the repair group and 35 ml per square meter in the replacement group, and equal 1-year mortality of 10 to 20% in the two groups.¹³⁻¹⁵ We planned one interim analysis using a group-sequential monitoring procedure with a Lan-DeMets stopping boundary and O'Brien-Fleming spending function.^{16,17} The primary null hypothesis was that there would be no between-group difference in the LVESVI at 12

months. We tested this hypothesis in an intention-to-treat analysis using a two-tailed Wilcoxon rank-sum test, at a 0.05 alpha level. This analysis accommodated nonignorable missing LVESVI outcomes owing to the death of patients by assigning deceased patients the worst ranks in order on the basis of the time of death. We used multiple imputation for data that were missing for reasons other than death to calculate the 12-month LVESVI on the assumption that the data were missing at random. We used the Hodges-Lehmann estimator to quantify between-group differences in the reduction of the LVESVI from baseline. Sensitivity analyses assessed the robustness of findings to protocol deviations, missing data, and mortality (for adjustment to the LVESVI).

We used the log-rank test to compare rates of major adverse cardiac or cerebrovascular events and death from any cause and used hazard ratios from Cox regression models to quantify relative risks. Poisson regression was used to test between-group differences in rates of adverse events. We used chi-square tests to compare between-group differences in functional status (NYHA and Canadian Cardiovascular Society classifications). We used the Minnesota Living with Heart Failure questionnaire and the physical and mental subscales of the Medical Outcomes Study 12-Item Short Form Health Survey (SF-12) to assess quality of life. We used t-tests to compare differences in mean quality-of-life scores among surviving patients at 12 months.

RESULTS

PATIENTS

From 2009 through 2012, we screened 3458 patients; 447 of these patients were eligible to participate in the study, and 251 underwent randomization (126 to mitral-valve repair and 125 to mitral-valve replacement) (Fig. S1 in the Supplementary Appendix, available at NEJM.org). The two groups had similar baseline characteristics (Table 1). The mean (\pm SD) LVESVI was 61.1 \pm 26.2 ml per square meter in the repair group and 65.7 \pm 27.4 ml per square meter in the replacement group ($P=0.17$). The echocardiography core laboratory confirmed the diagnosis of severe mitral regurgitation in 96% of the patients; the remaining 4% of the patients had moderate mitral regurgitation. The use of anti-

Table 1. Baseline and Operative Characteristics of the Patients.*

| Characteristic | Repair Group (N=126) | Replacement Group (N=125) | P Value |
|--|-------------------------|------------------------------|---------|
| Male sex — no. (%) | 77 (61.1) | 78 (62.4) | 0.83 |
| Age — yr | 69±10 | 68±9 | 0.36 |
| White race — no. (%)† | 104 (82.5) | 98 (78.4) | 0.40 |
| Hispanic ethnic group — no. (%)‡ | 13 (10.3) | 11 (8.8) | 0.68 |
| Medical and surgical history — no. (%) | | | |
| Diabetes | 48 (38.1) | 41 (32.8) | 0.41 |
| Renal insufficiency | 29 (23.0) | 40 (32.0) | 0.11 |
| Previous CABG | 24 (19.0) | 23 (18.4) | 0.90 |
| Previous PCI | 50 (39.7) | 40 (32.0) | 0.20 |
| Heart failure | 88 (69.8) | 92 (73.6) | 0.51 |
| Myocardial infarction | 99 (78.6) | 88 (70.4) | 0.14 |
| Atrial fibrillation | 45 (35.7) | 35 (28.0) | 0.19 |
| Implantable cardioverter-defibrillator | 23 (18.3) | 17 (13.6) | 0.31 |
| Stroke | 14 (11.1) | 11 (8.8) | 0.54 |
| Left ventricular ejection fraction — % | 42.4±12.0 | 40.0±11.0 | 0.10 |
| Effective regurgitant orifice area — cm ² | 0.40±0.17 | 0.39±0.11 | 0.64 |
| Grade on CCS angina scale — no. (%)‡ | | | 0.19 |
| No angina | 57 (45.2) | 70 (56.0) | |
| Grade III or IV | 31 (24.6) | 21 (16.8) | |
| NYHA class III or IV — no./total no. (%)§ | 72/125 (57.6) | 76/124 (61.3) | 0.55 |
| Minnesota Living with Heart Failure score¶ | 46.1±27.2 | 50.0±27.4 | 0.29 |
| Concomitant procedure — no. (%) | | | |
| CABG | 93 (73.8) | 94 (75.2) | 0.80 |
| Tricuspid-valve repair | 16 (12.7) | 22 (17.6) | 0.28 |
| Atrial maze | 15 (11.9) | 16 (12.8) | 0.83 |

* Plus-minus values are means ±SD. CABG denotes coronary-artery bypass grafting, and PCI percutaneous coronary intervention.

† Race or ethnic group was self-reported.

‡ Grades III or IV for the Canadian Cardiovascular Society (CCS) classification of angina are as follows: grade III, marked limitation of ordinary physical activity, with walking one or two blocks on the level and climbing one flight of stairs in normal conditions and at normal pace; grade IV, inability to carry on any physical activity without discomfort, and anginal syndrome may be present at rest.

§ New York Heart Association (NYHA) classes range from I to IV, with higher classes indicating worse condition.

¶ Scores on the Minnesota Living with Heart Failure questionnaire range from 0 to 105, with higher scores indicating worse condition.

ischemic medications and heart-failure therapies was similar in the two study groups.

Concomitant procedures were performed in 86.1% of the patients. Investigators used complete annuloplasty rings in all patients undergoing mitral-valve repair, with an average ring size of 28.4±1.9 mm for men and 27.2±1.6 mm for women. Among patients receiving valve replacements, 95.4% underwent a chordal-sparing pro-

cedure. Because of intraoperative complications 11 patients in the repair group underwent valve replacement, and 1 patient in the replacement group underwent repair.

LEFT VENTRICULAR DIMENSION AND FUNCTION

At 12 months, the mean LVESVI among surviving patients was 54.6±25.0 ml per square meter in the repair group and 60.7±31.5 ml per square

meter in the replacement group (mean change from baseline, -6.6 ml and -6.8 ml per square meter, respectively). The rate of death was 14.3% in the repair group and 17.6% in the replacement group (hazard ratio with repair, 0.79; 95% confidence interval [CI], 0.42 to 1.47; $P=0.45$ by the log-rank test). The rank-based assessment of LVESVI at 12 months after adjustment for death showed no significant between-group difference (z score, 1.33; $P=0.18$). The median between-group difference in the change in the LVESVI from baseline was only 2.1 ml per square meter (95% CI, -5.1 to 9.3), which ruled out any clinically relevant difference. The mean left ventricular ejection fraction at 12 months was $41.5\pm 10.8\%$ in the repair group and $37.8\pm 12.5\%$ in the replacement group.

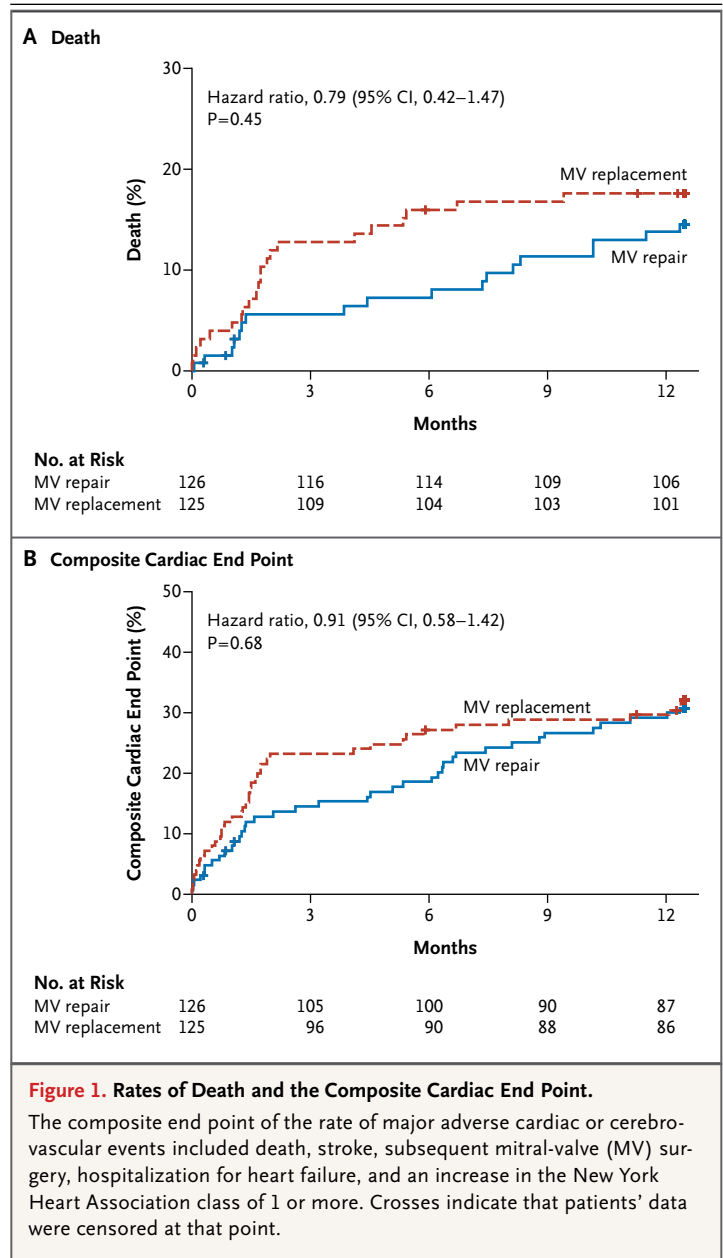
The proportion of surviving patients with a recurrence of moderate or severe mitral regurgitation at 12 months was significantly higher in the repair group than in the replacement group (32.6% [28.4% moderate and 4.2% severe] vs. 2.3% [all moderate]; $P<0.001$). In the repair group, the 12-month LVESVI was 64.1 ± 23.9 ml per square meter in patients with recurrent mitral regurgitation versus 47.3 ± 23.0 ml per square meter in those without recurrent mitral regurgitation ($P<0.001$). Within 1 year, three patients in the repair group and none in the replacement group underwent mitral-valve reoperation ($P=0.25$).

DEATH AND COMPOSITE CARDIAC END POINT

At 12 months, we observed no significant difference in cumulative mortality between the repair group and the replacement group (hazard ratio, 0.79; 95% CI, 0.42 to 1.47). The 30-day rate of death was 1.6% in the repair group (2 deaths) and 4.0% in the replacement group (5 deaths). Between 30 days and 1 year, 33 additional deaths occurred and were evenly distributed between the two study groups (Fig. 1A). The most frequent primary causes of death were multisystem organ failure (37.5%), heart failure (12.5%), and renal failure (10.0%). At 12 months, there was no significant between-group difference with respect to the composite end point of major adverse cardiac or cerebrovascular events (hazard ratio, 0.91; 95% CI, 0.58 to 1.42; $P=0.68$ by the log-rank test) (Fig. 1B) or any of its individual components (Table 2).

ADVERSE EVENTS AND HOSPITALIZATION

Rates of serious adverse events — most frequently, heart failure, arrhythmias, major local-



ized infection, and respiratory failure — did not differ significantly between the two study groups at 1 year (Table 2). The duration of the index hospitalization was similar in the repair and replacement groups (mean, 17.3 ± 11.4 days and 16.7 ± 10.4 days, respectively; $P=0.84$; and median, 14 days in each group). The mean length of stay after surgery was 11.5 ± 9.0 days in the repair group and 11.9 ± 8.6 days in the replacement group, with no significant between-group differences in rates of readmission.

Table 2. Clinical End Points, Serious Adverse Events, and Hospitalizations at 30 Days and 1 Year.

| Clinical end point | 30 Days | | | 1 Year | | |
|---------------------------------------|--|------------------------------|---------|--|------------------------------|---------|
| | Repair Group (N=126) | Replacement Group (N=125) | P Value | Repair Group (N=126) | Replacement Group (N=125) | P Value |
| | <i>no. of patients (%)</i> | | | <i>no. of patients (%)</i> | | |
| Death | 2 (1.6) | 5 (4.0) | 0.26 | 18 (14.3) | 22 (17.6) | 0.47 |
| Stroke | 3 (2.4) | 4 (3.2) | 0.72 | 6 (4.8) | 5 (4.0) | 0.77 |
| Worsening in NYHA class of 1 | 10 (7.9) | 10 (8.0) | 0.99 | 6 (4.8) | 6 (4.8) | 0.99 |
| Rehospitalization for heart failure | 3 (2.4) | 7 (5.6) | 0.22 | 17 (13.5) | 14 (11.2) | 0.58 |
| Mitral-valve reoperation | 1 (0.8) | 0 | 1.0 | 3 (2.4) | 0 | 0.25 |
| Composite major adverse event* | 19 (15.1) | 24 (19.2) | 0.39 | 41 (32.5) | 42 (33.6) | 0.86 |
| | <i>no. of events (rate/100 patient-yr)</i> | | | <i>no. of events (rate/100 patient-yr)</i> | | |
| Serious adverse event | | | | | | |
| Any | 115 (1102.2) | 131 (1277.3) | 0.25 | 221 (202.1) | 194 (189.0) | 0.49 |
| Heart failure | 10 (95.8) | 10 (97.5) | 0.97 | 33 (30.2) | 21 (20.5) | 0.16 |
| Stroke | 3 (28.8) | 4 (39.0) | 0.69 | 6 (5.5) | 5 (4.9) | 0.84 |
| Other neurologic dysfunction | 3 (28.8) | 2 (19.5) | 0.67 | 4 (3.7) | 2 (2.0) | 0.46 |
| Myocardial infarction | | | | | | |
| Nonoperative | 1 (9.6) | 0 | 0.32 | 3 (2.7) | 0 | 0.08 |
| Perioperative | 0 | 2 (19.5) | 0.16 | 0 | 2 (2.0) | 0.16 |
| Renal failure | 3 (28.8) | 9 (87.8) | 0.08 | 4 (3.7) | 10 (9.7) | 0.09 |
| Bleeding | 6 (57.5) | 9 (87.8) | 0.42 | 6 (5.5) | 10 (9.7) | 0.26 |
| Arrhythmia | | | | | | |
| Supraventricular | 15 (143.8) | 14 (136.5) | 0.89 | 21 (19.2) | 18 (17.5) | 0.78 |
| Ventricular | 8 (76.7) | 11 (107.3) | 0.47 | 12 (11.0) | 12 (11.7) | 0.88 |
| Localized infection | 9 (86.3) | 13 (126.8) | 0.37 | 16 (14.6) | 21 (20.5) | 0.31 |
| Sepsis | 3 (28.8) | 1 (9.8) | 0.32 | 11 (10.1) | 5 (4.9) | 0.16 |
| Respiratory failure | 10 (95.8) | 16 (156.0) | 0.22 | 14 (12.8) | 18 (17.5) | 0.38 |
| Hospitalization | | | | | | |
| Any rehospitalization | 15 (235.6) | 27 (456.6) | 0.04 | 106 (102.9) | 85 (88.2) | 0.29 |
| Readmission for cardiovascular causes | 6 (94.3) | 14 (236.7) | 0.05 | 56 (54.4) | 38 (39.4) | 0.12 |

* The composite major adverse event was death, stroke, hospitalization for heart failure, worsening heart failure, or mitral-valve reintervention.

QUALITY OF LIFE

There was no significant difference between the two study groups with respect to any measure of quality of life or functional status at 12 months (Table 3). As measured on the Minnesota Living with Heart Failure questionnaire, there was a reduction from baseline in heart-failure symptoms

of 46.9% in the repair group and 61.2% in the replacement group. Similarly, as measured by means of the score on the SF-12 physical subscale, there was improvement over baseline in physical health of 16.6% in the repair group and 18.4% in the replacement group. Figure 2 shows NYHA classification and mortality over time.

Table 3. Quality of Life and Functional Status of Patients at 1 Year.*

| Scale | Repair Group | Replacement Group | P Value |
|---|----------------|-------------------|---------|
| SF-12† | | | |
| Physical function | | | 0.63 |
| Score | 43.6±8.1 | 44.2±7.1 | |
| Patients evaluated — no./total no. (%) | 93/105 (88.6) | 85/102 (83.3) | |
| Mental function | | | 0.92 |
| Score | 46.8±7.1 | 46.9±6.4 | |
| Patients evaluated — no./total no. (%) | 93/105 (88.6) | 85/102 (83.3) | |
| Minnesota Living with Heart Failure questionnaire | | | |
| Score | 24.5±23.1 | 19.6±19.4 | 0.12 |
| Patients evaluated — no./total no. (%) | 95/105 (90.5) | 85/102 (83.3) | |
| EQ-5D‡ | | | |
| Score | 73.7±16.3 | 73.9±20.1 | 0.97 |
| Patients evaluated — no./total no. (%) | 91/105 (86.7) | 80/102 (78.4) | |
| NYHA class — no./total no. (%) | | | |
| All classes | 100/105 (95.2) | 93/102 (91.2) | 0.28 |
| Class III or IV | 9/100 (9.0) | 13/93 (14.0) | |
| CCS classification — no./total no. (%) | | | |
| All classes | 96/105 (91.4) | 89/102 (87.3) | 0.42 |
| Class III or IV | 3/96 (3.1) | 2/89 (2.2) | |

* Plus–minus values are means ±SD.

† Scores on the Medical Outcomes Study 12-Item Short Form Health Survey (SF-12) range from 0 to 100, with higher scores indicating a better outcome.

‡ Scores on the EuroQol Group 5-Dimension Self-Report Questionnaire (EQ-5D) range from 0 to 100, with higher scores indicating a better quality of life.

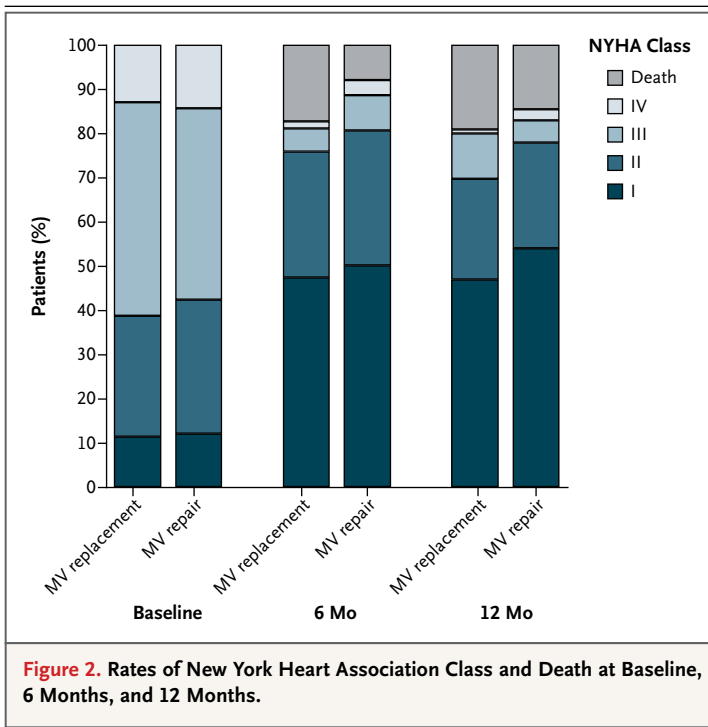
DISCUSSION

The most effective surgical approach to the treatment of severe ischemic mitral regurgitation remains controversial. In the past few years, the use of mitral-valve repair has greatly exceeded the use of replacement.¹⁸ However, no randomized trials have established the superiority of repair across a spectrum of patients with severe ischemic mitral regurgitation.

Left ventricular remodeling, as measured by means of the LVESVI (the primary end point in our trial), is a predictor of poor prognosis among patients with ischemic myocardial disease, and efforts to reverse such remodeling have been associated with improved outcomes.^{19–21} In our study, the two surgical approaches reduced the LVESVI at 12 months, although there was no significant between-group difference. Moreover, there were no significant differences in mortal-

ity at 30 days or 12 months. The observed 30-day rates of death (1.6% in the repair group and 4.0% in the replacement group) were lower than the national rates reported by the Society of Thoracic Surgeons (5.3% and 8.5% for repair and replacement with CABG, respectively).²²

Our findings contradict much of the published literature on this topic, which reports several advantages to mitral-valve repair over replacement, including lower operative mortality, improved left ventricular function, and higher rates of long-term survival.^{23–26} In particular, in a recent meta-analysis,²⁷ the relative long-term risk of death was 35% higher in the replacement group than in the repair group. Patients undergoing mitral-valve replacement tend to be older and have more coexisting illnesses than those undergoing repair, so adjustment for baseline differences has been critical in nonrandomized studies. Yet even these methods cannot adjust



for differences when particular risk factors are unknown or unmeasured, which may explain why some studies have shown no differences in short-term or long-term rates of survival between repair and replacement groups,²⁸ whereas a majority of studies have favored repair. The evolution of valve replacement with chordal sparing may account for the improved results we observed, as compared with previous studies, since the retention of the internal architectural support of the left ventricle may preserve contractile efficiency and reduce left ventricular dilatation and dysfunction.

Our trial confirmed an excess incidence of recurrence of mitral regurgitation at 1 year among patients undergoing mitral-valve repair. Among survivors, the rate of moderate or severe recurrent mitral regurgitation at 1 year was 30 percentage points higher among patients who underwent repair than among those who underwent replacement. Our findings are similar to those reported in previous studies, in which the 6-month prevalence of mitral regurgitation of 2+ or more after repair was 15 to 25% and increased substantially over time.^{29,30} The patients with recurrence in the repair group showed no reverse remodeling, as compared with those without recurrence (LVESVI of 64.1±23.9 and 47.3±23.0,

respectively). This lack of durability in correction of mitral regurgitation is disconcerting, given its reported association with further progression and long-term negative outcomes.^{4,31,32}

The high rate of recurrence of mitral regurgitation in the repair group did not correspond with significant differences in the overall composite end point of major adverse cardiac or cerebrovascular events, quality of life, or functional status at 12 months. Similarly, rates of serious adverse events and hospital readmissions did not differ significantly between groups.

The baseline LVESVI that we observed was lower than we had assumed it would be, reflecting variability in left ventricular size and severity of mitral regurgitation in these patients, along with inconsistent methods that were used to assess mitral regurgitation in previous studies. Although the baseline LVESVI was lower than assumed, so too was its variability, with the statistical power for the study remaining at 90%. The mitral regurgitation in patients enrolled in this trial was entirely ischemic in nature and was severe (in 96% of the patients) according to integrative echocardiographic criteria, and the baseline ejection fraction was similar to that reported previously.³³ The mean effective regurgitant orifice area among patients in our study was 0.4 cm², which qualifies as severe mitral regurgitation according to the recent guidelines of the European Society of Cardiology, which provide a threshold of 0.2 cm². The patients in our study had a relatively long length of stay during the index hospitalization, with the majority of the stay occurring after surgery. This duration may reflect the patients' relatively high rates of respiratory failure, bleeding, and supraventricular arrhythmia in the first 30 days, complications that provide targets for quality-improvement measures.

Our trial has several limitations. First, although it assesses surgical approaches to the mitral valve, it does not evaluate the strategy of revascularization alone. Given current guidelines, there was lack of equipoise to randomly assign patients with severe mitral regurgitation to a CABG-only group. However, there is equipoise for the randomization of patients with moderate ischemic mitral regurgitation to revascularization alone, and such a CTSN trial is ongoing (ClinicalTrials.gov number, NCT00806988). Second, the primary end point was an echocar-

diographic measure of left ventricular remodeling, not a clinical outcome such as survival. However, a randomized trial with a 1-year mortality end point would have required more than 4000 patients, exceeding our capacity for timely enrollment. Our choice of the LVESVI as the primary end point was driven by strong evidence correlating the LVESVI with clinical outcomes, including the NYHA class and rates of hospitalization and survival.³⁴⁻⁴⁰ Third, the use of transthoracic echocardiography for measuring recurrent mitral regurgitation may underestimate the degree of mitral regurgitation in patients with prosthetic valves. However, the transmitral gradient, and thus the inflow velocity, that were observed in these patients were within normal ranges, which suggests no substantial mitral regurgitation. Finally, we report here on a relatively short follow-up period of 12 months, although follow-up will continue for 24 months.

Recently, the field has embraced mitral-valve repair over replacement, without a strong evidence base. According to 2008–2012 data from the Society of Thoracic Surgeons, 66% of mitral-valve surgeries in patients undergoing CABG

used a repair approach.⁴¹ However, our comparison between chordal-sparing mitral-valve replacement and repair in patients with severe ischemic mitral regurgitation did not show significant differences. This conclusion is based on the absence of a significant difference in left ventricular reverse remodeling and in the rate of major adverse cardiac or cerebrovascular events at 12 months. Mitral-valve replacement provides a considerably more durable correction of mitral regurgitation, which may have an important effect on long-term outcomes. However, this factor must be weighed against any potential adverse consequences of a prosthetic valve. Further patient follow-up is needed to confirm the findings of this trial; such follow-up may lead to the identification of predictors of recurrence of mitral regurgitation to allow for a more appropriate selection of patients.

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APPENDIX

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