Outcomes of coronary artery bypass grafting and reduction annuloplasty for functional ischemic mitral regurgitation: A prospective multicenter study (Randomized Evaluation of a Surgical Treatment for Off-Pump Repair of the Mitral Valve)

Eugene A. Grossi, MD,[a] Y. Joseph Woo, MD,[b] Nirav Patel, MD,[c] Judith D. Goldberg, ScD,[a] Charles F. Schwartz, MD,[a] Valavanur A. Subramanian, MD,[c] Christopher Genco, MD,[d] Scott M. Goldman, MD,[e] Marco A. Zenati, MD,[f] J. Alan Wolfe, MD,[g] Yugal K. Mishra, MD,[h] and Naresh Trehan, MD[i]

Objective: Functional ischemic mitral regurgitation is a complication of ventricular remodeling; standard therapy is reduction annuloplasty and coronary artery bypass grafting. Unfortunately, outcomes are retrospective and contradictory. We report a multicenter study that documents the outcomes of reduction annuloplasty for functional ischemic mitral regurgitation.

Methods: Twenty-one centers randomized 75 patients to the coronary artery bypass grafting + reduction annuloplasty subgroup that was the control arm of the Randomized Evaluation of a Surgical Treatment for Off-pump Repair of the Mitral Valve trial. Entry criteria included patients requiring revascularization, patients with severe or symptomatic moderate functional ischemic mitral regurgitation, an ejection fraction 25% or greater, a left ventricular end-diastolic dimension 7.0 cm or less, and more than 30 days since acute myocardial infarction. All echocardiograms were independently scored by a core laboratory. Reduction annuloplasty was achieved by device annuloplasty. Two patients underwent immediate intraoperative conversion to a valve replacement because reduction annuloplasty was unable to correct mitral regurgitation; as-treated results are presented.

Results: Thirty-day mortality was 4.1% (3/73). Patients received an average of 2.8 bypass grafts. Mean follow-up was 24.6 months. Mitral regurgitation was reduced from 2.6 ± 0.8 preoperatively to 0.3 ± 0.6 at 2 years. Freedom from death or valve reoperation was $78\% \pm 5\%$ at 2 years. There was significant improvement in ejection fraction and New York Heart Association class with reduction of left ventricular end-diastolic dimension. Cox regression analyses suggested that increasing age ($P = .001$; hazard ratio, 1.16 per year; 95% confidence interval, 1.06–1.26) and renal disease ($P = .018$; hazard ratio, 3.48; 95% confidence interval, 1.25–9.72) were associated with decreased survival.

Conclusions: Coronary artery bypass grafting + reduction annuloplasty for functional ischemic mitral regurgitation predictably reduces mitral regurgitation and relieves symptoms. This treatment of moderate to severe mitral regurgitation is associated with improved indices of ventricular function, improved New York Heart Association class, and excellent freedom from recurrent mitral insufficiency. Although long-term prognosis remains guarded, this multicenter study delineates the intermediate-term benefits of such an approach. (J Thorac Cardiovasc Surg 2011;141:91-7)

From the New York University School of Medicine,[a] New York, NY; Hospital of the University of Pennsylvania,[b] Philadelphia, Pa; Lenox Hill Medical Center,[c] New York, NY; Covenant Health Center,[d] Saginaw, Mich; Lankenau Hospital,[e] Lancaster, Pa; Veterans Administration Hospital,[f] Pittsburgh, Pa; St Joseph's Hospital,[g] Atlanta, Ga; Escorts Heart Institute and Research Centre,[h] New Delhi, India; and Indrapratha Apollo,[i] New Delhi, India.

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Address for reprints: Eugene A. Grossi, MD, NYU Medical Center, Suite 9-V, 530 First Avenue, New York, NY 10016 (E-mail: Eugene.grossi@nyumc.org).

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Functional ischemic mitral regurgitation (FIMR) is a frequent end-stage complication of coronary artery disease caused by ventricular remodeling. With increasing ventricular size, the mitral annulus dilates and papillary muscle displacement tethers leaflets, causing functional mitral regurgitation (FMR). This further impairs ventricular function with the progression of negative left ventricular (LV)

Abbreviations and Acronyms

CABG = coronary artery bypass grafting
CI = confidence interval
FDA = Food and Drug Administration
FIMR = functional ischemic mitral regurgitation
FMR = functional mitral regurgitation
HR = hazard ratio
LV = left ventricular
LVED = left ventricular end diastolic
MR = mitral regurgitation
RA = reduction annuloplasty

remodeling.[1,2] Current treatments for LV dysfunction with FMR include medical therapy and surgery. With viable ischemic myocardium, revascularization prevents further damage, relieves the contributing ischemia, and may stop or reverse the remodeling process. The effect of correcting the ischemia alone on valve function has been unpredictable and often transient, leaving the majority of patients with residual, recurrent, or progressive mitral regurgitation (MR).[3] Significant MR is treated by valve repair or replacement. Mitral repair is primarily done with a reduction annuloplasty (RA), whereby an undersized annuloplasty device increases the coaptive leaflet margin and eliminates regurgitation.[4] Current surgical techniques for FMR have significant procedural risk, and the late outcomes remain guarded.[5] Although valve repair is generally believed to be superior to replacement, replacement is sometimes recommended in patients with significant leaflet tethering who are considered high risk for recurrence.[6]

Thus, the gold standard therapy for FIMR is RA and coronary artery bypass grafting (CABG) when appropriate. Outcome data are retrospective, limited to individual series, and somewhat contradictory. This report details a prospective, multicenter, independently monitored and audited study that documents the outcomes of RA for FIMR using core laboratory reviewed data.

MATERIALS AND METHODS

Twenty-one centers (Appendix 1) randomized 75 patients to a CABG+RA as a stratum in the control arm of the Randomized Evaluation of a Surgical Treatment for Off-pump Repair of the Mitral Valve trial. This Food and Drug Administration (FDA)-approved investigational device trial (Clinical Trials ID = NCT00120276) compared CABG plus ventricular reshaping (Coapsys; Myocor Inc, Maple Grove, Minn) with CABG+RA; the primary, comparative outcomes have been reported.[7] Patients were on average 65.8 years old and predominately male (86.3%). Table 1 contains patient demographic information for the 75 randomized patients. The FDA's study entry criteria favored the exclusion of particularly high-risk surgical candidates to evaluate differences in midterm survival. Entry criteria included patients requiring revascularization, patients with severe FIMR (or symptomatic moderate FIMR), an ejection fraction 25% or greater, an LV end-diastolic (LVED) dimension 7.0 cm or less, and more than 30 days since an acute transmural myocardial infarction. Appendix 2 shows full inclusion/exclusion criteria. All echocardiograms were independently reviewed and scored by a core laboratory (Mayo Clinic). MR severity was graded as 0 = none, 1 = mild, 2 = moderate, 3 = moderate–severe, and 4 = severe. RA was achieved by band or ring annuloplasty; the type of annuloplasty device was chosen at the surgeon's discretion. Two patients underwent intraoperative conversion to chordal sparing mitral valve replacement due to an inability to correct MR with RA. The as-treated results are presented.

This study was approved by each participating medical center's institutional review board. Adverse events were adjudicated by an independent Clinical Events Committee, and results were monitored by a Data Safety Monitoring Board. The trial was initiated as a feasibility study in April 2003 and expanded with FDA approval into a pivotal study in June 2004. This study was prematurely terminated when the sponsor failed to secure ongoing funding in October 2008. At the time of closure, 165 patients had been randomized. Mean follow-up was 24.6 months. The database was maintained in Clindex (FORTRESS Medical Systems, Hopkins, MN), and statistical analyses, such as mixed model and multivariable Cox regression, were performed using SAS (SAS Institute Inc, Cary, NC) and SPSS (SPSS Inc, Chicago, IL). Mean and standard deviations are reported.

RESULTS

Operative mortality was 4.1% (3/73). Patients received a mean of 2.8 bypass grafts. Multivariable Cox regression analyses revealed that older age ($P = .001$; hazard ratio [HR] = 1.16/y; 95% confidence interval [CI], 1.06–1.26) and the presence of renal disease ($P = .018$; HR = 3.48; 95% CI, 1.25–9.72) were associated with decreased survival. Renal disease ($P = .007$; HR = 3.8; 95% CI, 1.5–10.0), older age ($P = .055$; HR = 1.1, 95% CI, 0.99–1.1), and LV end-systolic volume index ($P = .091$, HR = 1.02, 95% CI, 0.99–1.04) were associated with decreased freedom from death, reoperation, or recurrent MR (moderate or worse).

MR severity was significantly reduced from 2.54 ± 0.80 at baseline to 0.52 ± 0.66 and 0.35 ± 0.63 at 1 and 2 years, respectively (Table 2). Two patients had RA performed without impact on MR grade and had to be intraoperatively converted to mitral replacement; these patients were excluded from this as-treated analysis. In total, 12 patients (16.1%) had moderate or worse recurrent MR during follow-up. The technical details of these patients are included in Appendix 3.

Five patients had moderate MR at discharge and a 48% 2-year survival; however, this was not statistically significant when compared with all patients ($P = .45$). One patient had recurrent MR (mild at discharge and moderate–severe at 1 year) with reoperative valve replacement at 15 months. This patient's baseline LVED dimension was 6.3 cm with a baseline ejection fraction of 40%.

Table 3 summarizes the functional and dimensional changes. Ejection fraction significantly improved from 38% to 47% at 2 years. Reverse remodeling was evident with significant decreases in end-diastolic and end-systolic dimensions. New York Heart Association class significantly improved in the majority of patients; 65.9% improved 1 or more grades at 1 year and 72.0% at 2 years.