Functional impact of transmitral gradients at rest and during exercise after restrictive annuloplasty for ischemic mitral regurgitation

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Objectives: Restrictive mitral valve annuloplasty combined with coronary artery bypass grafting is the treatment of choice for ischemic mitral regurgitation. Postoperative functional mitral stenosis and its potential impact on functional capacity remain the object of debate. The aim of this study was to assess functional and hemodynamic outcome at rest and during exercise in a population with ischemic mitral regurgitation after a standardized restrictive mitral valve annuloplasty.

Methods: A total of 23 patients with ischemic mitral regurgitation who were previously treated with coronary artery bypass grafting and restrictive mitral valve annuloplasty underwent a semi-supine (bicycle) exercise test with Doppler echocardiography and ergospirometry. The surgical technique was identical in all patients, using a complete semi-rigid ring downsized by 2 sizes after measuring the height of the anterior mitral leaflet, to achieve a coaptation length of at least 8 mm.

Results: At a mean follow-up of 28 $\pm$ 15 months, mean transmitral gradients at rest and maximal exercise were 4.4 $\pm$ 1.8 mm Hg and 8.2 $\pm$ 4.2 mm Hg, respectively ($P < .001$). Transmitral gradients did not correlate with exercise capacity (maximal oxygen uptake) or pulmonary artery pressures. Patients with a resting mean gradient of 5 mm Hg or greater ($n = 9$) reached a significantly higher maximal oxygen uptake; however, they had a better ejection fraction and cardiac output at rest and reached a higher cardiac output at peak exercise.

Conclusions: Transmitral gradients after restrictive mitral valve annuloplasty for ischemic mitral regurgitation did not correlate with functional capacity as measured by maximal oxygen uptake during semi-supine bicycle testing. Functional capacity and transmitral gradients are determined not only by the severity of mitral stenosis but also by hemodynamic factors, such as ejection fraction and cardiac output. Transmitral gradients should be interpreted with respect to patient hemodynamics and not necessarily be considered as detrimental for functional capacity. (J Thorac Cardiovasc Surg 2014;148:183-7)

ACD

Restrictive mitral valve annuloplasty (RMA) has become the preferred surgical approach in the management of ischemic mitral regurgitation (IMR) on the basis of good short- and mid-term data from observational studies.[1-3] RMA involves the insertion of an undersized prosthetic ring, thereby reducing anteroposterior dimensions of the mitral annulus, resulting in improved leaflet coaptation. At mid-term follow-up, this procedure has been shown to induce significant reverse remodeling and improve systolic function, making it an effective strategy for patients with severe IMR.[3] However, several recent studies have demonstrated the occurrence of moderate "functional" mitral stenosis (MS) after RMA, that is, a mean transmitral pressure gradient greater than 5 mm Hg or a mitral valve area less than 1.5 cm^2, with incidences of MS ranging from 9%[4] to 54%[5] after RMA. The impact of a postoperative MS on functional and clinical outcome remains controversial. Magne and colleagues[6] demonstrated a significant negative correlation between mitral peak gradient at rest and 6-minute walking test distance, suggesting a deleterious effect on functional capacity. Other studies have failed to demonstrate an effect of transmitral gradients on survival,[5,7,8] adverse cardiac events,[4] or New York Heart Association functional class.[7] In many of those patient groups, operative techniques and surgical end points of RMA were heterogeneous and nonstandardized. The aim of the current study was to assess functional capacity and hemodynamic outcome in a homogeneous population

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Abbreviations and Acronyms

CABG	= coronary artery bypass grafting
ICU	= intensive care unit
IMR	= ischemic mitral regurgitation
IQR	= interquartile range
LV	= left ventricular
MR	= mitral regurgitation
MS	= mitral stenosis
PAP	= pulmonary artery pressure
RMA	= restrictive mitral valve annuloplasty
VO_2max	= maximal oxygen uptake

with IMR after a standardized RMA, with a target postoperative coaptation length of at least 8 mm.

MATERIALS AND METHODS

Study Population

Between July 2007 and August 2012, 52 standardized RMA procedures in patients with IMR have been performed in our center. These procedures comprised all urgent (within 72 hours of admission), semi-urgent (within 14 days during the same hospital stay), and elective procedures. At 39 ± 15 months postoperatively, all survivors (n = 34) were contacted to undergo a resting echocardiography followed by an exercise stress echocardiography with ergospirometry, as approved by the local ethics committee. Written informed consent was obtained from all of the participating patients. Figure 1 displays the study flow chart, with 11 patients refusing participation for various reasons. The final study population consisted of 23 patients with IMR who were previously treated with coronary artery bypass grafting (CABG) and standardized RMA and who underwent a single study visit at our center with resting and exercise echocardiography.

Surgical Procedure

All surgical procedures were performed through a midline sternotomy under normothermic cardiopulmonary bypass with intermittent antegrade warm blood cardioplegia. After the revascularization procedure, the mitral valve was exposed through a vertical trans-septal approach. Mitral annuloplasty ring size was determined after careful measurement of the height of the anterior leaflet and downsized by 2 sizes with a complete semi-rigid annuloplasty ring (Carpentier-Edwards Physio Ring I; Edwards Lifesciences, Irvine, Calif). A saline test was performed to check the symmetric and posteriorly located line of coaptation. After weaning from cardiopulmonary bypass, intraoperative transesophageal echocardiography was used to assess the result and to measure leaflet coaptation. A minimum coaptation length of 8 mm in the A2-P2 segment was pursued.

Transthoracic Echocardiography

Preoperative 2-dimensional echocardiography examinations were retrospectively analyzed for comparison with the echocardiographic data at the follow-up visit. The postoperative mean transmitral gradient from all patients (also patients not participating in the exercise echocardiography) was retrospectively measured from 2-dimensional echocardiography, which was systematically performed immediately after intensive care unit (ICU) discharge. All echocardiographic examinations were performed with a commercially available system (IE33; Philips Healthcare, Andover, Mass) and with standard 2-dimensional and Doppler echocardiographic images acquired in the left lateral decubitus position using a phased-array transducer in the parasternal and apical views by experienced cardiac sonographers. At the study visit, 3 consecutive cardiac cycles were recorded and stored for subsequent offline analysis. Left ventricular (LV) end-diastolic and end-systolic dimensions were measured from parasternal acquisitions. LV volumes and ejection fraction were calculated using the modified Simpson's biplane method. LV stroke volume was measured by pulsed-wave Doppler in the LV outflow tract. Color flow was applied in the apical 4-chamber view to assess the severity of mitral regurgitation (MR), which was graded by the vena contracta width. Peak and mean transmitral gradients were calculated using the modified Bernoulli equation on the continuous-wave signal. Systolic pulmonary artery pressure (PAP) was calculated using the modified Bernoulli equation on the transtricuspid continuous-wave Doppler signal, while adding right atrial pressure.[9]

Exercise Protocol

All 23 patients underwent a symptom-limited graded bicycle test in a semi-supine position on a tilting exercise table. Workload was initiated at 20 Watts, with increments of 20 Watts every 3 minutes. In patients with poor general condition, an adjusted protocol was applied with 10 Watts of initial workload and increments of 10 Watts every 3 minutes. Blood pressure and a 12-lead electrocardiogram were recorded at each stage. Two-dimensional and Doppler echocardiographic recordings were made at each stage, that is, for measuring LV geometry and function, LV stroke volume, MR vena contracta width, peak and mean transmitral gradient, and systolic PAP.

Cardiopulmonary Exercise Testing

Real-time ergospirometry data were assessed using a commercially available system (JAEGER, Würzburg, Germany). Maximal oxygen uptake (VO_2max) during exercise was assessed in all patients.

Statistical Analysis

Results are expressed as mean ± standard deviation if normally distributed or otherwise by median and interquartile range (IQR). Normality was assessed by the Shapiro–Wilk statistic. The paired Student *t* test and Wilcoxon signed-rank test were used when appropriate to compare between preoperative and postoperative echocardiographic parameters and between resting and exercise data in the postoperative setting. Categoric values were compared using the Pearson chi-square test when appropriate. Cumulative survival curves were calculated according to the Kaplan–Meier method, and survival in high versus low gradient groups was compared with the log-rank test. Statistical significance was set at a 2-tailed probability of $P < .05$. Statistical analyses were performed using the Statistical Package for Social Sciences release 20.0 (SPSS Inc, Chicago, Ill).

RESULTS

Preoperative and Operative Clinical Data

Preoperative patient characteristics are summarized in Table 1. The patient population consisted of 23 patients with IMR, with a median ring size of 26 (IQR, 26-28) and a median postoperative coaptation length of 8.8 mm (IQR, 7.6-9.0 mm). In 3 of 23 patients (12%), a concomitant aneurysmectomy was performed, and 3 of 23 patients (12%) received a cardiac resynchronization therapy device before our study follow-up examination.

Comparison of Preoperative Versus Postoperative (Follow-up) Echocardiography

At a mean follow-up of 28 ± 15 months, in the group of 17 patients without aneurysmectomy and cardiac