Reduction of Mitral Valve Leaflet Tethering by Procedures Targeting the Subvalvular Apparatus in Addition to Mitral Annuloplasty

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Background: Ischemic mitral regurgitation (IMR) with ischemic cardiomyopathy (ICM) was treated with surgical procedures, and mitral leaflet tethering was assessed. Twenty-two patients with both ICM (left ventricular ejection fraction <0.35) and IMR (≥2) underwent coronary artery bypass grafting (CABG), mitral annuloplasty (MAP) with or without surgical ventricular restoration (SVR) and procedures targeting the subvalvular apparatus.

Methods and Results: Fourteen patients (group 1) underwent CABG and MAP, and the remaining 8 (group 2) underwent CABG, MAP, SVR, papillary muscle approximation (PMA), and papillary muscle suspension (PMS). PMA joined the entire papillary muscles with 3 mattress sutures. For PMS, 2 ePTFE sutures were placed between papillary muscle tips and fibrous annuli. Anterior and posterior mitral leaflet tethering angles (ALA and PLA) relative to the line connecting annuli, posterior and apical displacement of coaptation, and IMR grade were measured on echocardiography. Although preoperative ALA and PLA in group 2 were significantly larger than in group 1, there was no significant difference between groups at 1 month after surgery. At 1 year after surgery, however, the situation reversed: ALA and PLA in group 1 were significantly larger than in group 2.

Conclusions: In addition to MAP, procedures targeting the subvalvular apparatus including PMA and PMS achieved persistent reduction of mitral valve leaflet tethering, which might lead to the improvement of long-term outcome. (Circ J 2013; 77: 1461–1465)

Key Words: Ischemic heart disease; Mitral valve repair; Myocardial remodeling

After myocardial infarction, the left ventricle (LV) undergoes remodeling, the annulus dilates, the papillary muscles become tethered, and the distance between papillary muscles can increase, which leads to incomplete closure of mitral leaflets and the development of ischemic mitral regurgitation (IMR), which is associated with poor prognosis. Restrictive mitral annuloplasty (RMA) combined with coronary artery bypass grafting (CABG) may provide good results in selected patients, that is, in patients with mildly or moderately dilated ventricles and with mild to moderate alteration of mitral valve geometry, but this procedure is associated with a high rate of persistent/recurrent MR and with a lack of survival benefit in the other patients. Hence, mitral valve replacement with chordal sparing or alternative procedures targeting the mitral valve apparatus and/or the LV should be contemplated in the patients identified as having a high risk of RMA failure based on preoperative assessment.

In this study, we evaluated mitral valve function on echocardiography in a group of patients who underwent papillary muscle approximation (PMA) and suspension (PMS) in addition to CABG, mitral annuloplasty (MAP), and surgical ventricular restoration (SVR). The aim of the study was to compare the mitral valve function between the groups with or without procedures targeting the mitral valve apparatus and the LV.

Methods

Between January 2007 and June 2012, 22 patients (19 men and 3 women; mean age, 64.2 years) who had both ischemic cardiomyopathy with <35% left ventricular ejection fraction (LVEF) and IMR ≥ grade 3 were enrolled in this study. All patients underwent CABG with arterial and venous grafts and MAP. Of them, 14 patients (group 1) whose left ventricular end-systolic volume index (LVESVI) was <100 ml/m² underwent CABG, MAP, SVR according to endo-ventricular circular patch plasty, PMA, and suspension. The remaining 8 patients (group 2) whose LVESVI was ≥100 ml/m² underwent CABG, MAP, SVR alone. The remaining 8 patients (group 2) whose LVESVI was ≥100 ml/m² underwent CABG, MAP, SVR according to endo-ventricular circular patch plasty, PMA,
and PMS for the specific procedures targeting the subvalvular apparatus.

Mean preoperative LVEF indicated significantly poorer LV function in group 2 (21.4%±8.5%), compared to group 1 (29.0%±9.3%, P<0.05) and, according to the preoperative LV volume data, group 2 had significantly larger LV volume compared to group 1: LVESVI, 95.1±12.5 ml/m² in group 1 and 125.5±15.3 ml/m² in group 2 (P<0.05); LV end-diastolic volume index (LVEDVI), 130.0±16.5 ml/m² in group 1 and 151.0±18.8 ml/m² in group 2 (P<0.05); LV diastolic dimension, 62.3±7.8 mm in group 1 and 70.3±5.4 mm in group 2 (P<0.05); and LV systolic dimension, 52.4±7.5 mm in group 1 and 59.7±6.3 mm in group 2 (P<0.05). Preoperative risk factors included renal dysfunction (serum creatinine >2.0) for 4 patients, and emergency surgery was performed in 2 patients. Preoperative New York Heart Association functional class was III in 14 and IV in 8, including 2 patients who were catecholamine dependent and 7 patients who had preoperative prophylactic intraaortic balloon pump support (Table 1).

### Table 1. Patient Profiles

|                      | Group 1 | Group 2 |
|----------------------|---------|---------|
| n                    | 14      | 8       |
| Age (years)*         | 58.4±6.9| 69.3±7.7|
| Hypertension         | 8       | 4       |
| Diabetes             | 9       | 4       |
| Hyperlipidemia       | 6       | 6       |
| Renal dysfunction    | 2       | 2       |
| Stroke               | 2       | 2       |
| Peripheral artery disease | 2   | 0   |
| Emergency            | 1       | 1       |
| Intra-aortic balloon pump | 4  | 3   |
| Catecholamine dependance | 1 | 1 |
| Ventricular arrhythmia | 1 | 3 |
| Operation time (min) | 431±75.8| 426±85.6|
| Extracorporeal circulation (min)* | 169±26.1| 212±46.9|
| Aorta clamp time (min)* | 121±47.2| 150±40.0|

Data given as n or mean±SD. *P<0.05 (comparison between groups 1 and 2).

Surgical Technique

After a median sternotomy, moderate hypothermic cardiopulmonary bypass was achieved through aortic and bivacal cannulation. Both antegrade and retrograde cold-blood cardioplegia were used for myocardial protection. Once the mitral valve was exposed through a right side incision, the valve was inspected and the pathophysiology was confirmed. Several 2-0 braided polyester sutures in the whole annulus were used for rigid ring annuloplasty with Physio II (Edwards life sci., CA, USA). Our preference of the selection of the ring size was similar to the ring sizers, and 28-mm rings (18 patients) or 30-mm rings (4 patients) were used.

In group 2, the LV was opened from the center of the scarred tissue. When the infarction was anterolateral and septal, the incision was made parallel to the left anterior descending artery (surgical anterior ventricular endocardial restoration: SAVE procedure). When the infarction was antero-apical, the incision was made at the apex (Dor’s procedure).

With regard to the procedures targeting the subvalvular apparatus in group 2, PMA joined the entire papillary muscles from their base to their heads with 3 pledged mattress sutures of 3-0 prolene. Then, shortening of the distance between the anterolateral and postero-medial papillary muscles reduced the lateral and backward tethering of the mitral valve. PMS fixed the distance between the papillary muscles’ heads and the mitral annuli. This adjunctive method placed a subvalvular CV4 ePTFE suture between the chordal attachment site of the papillary muscles and the annuli at the center of the posterior and the anterior mitral leaflets. These sutures were passed through the annuloplasty ring. After tying all of the sutures for the annuloplasty ring, CV4 ePTFE sutures were pulled upward and tied after the LV was filled with a large quantity of saline solution. For closing the orifice and reconstructing the LV, an oval or circular woven Dacron patch was anchored to the fibrotic tissue. Finally, to improve hemostasis and reinforce the suture lines, the excluded fibrotic tissue was sewn with Teflon felt strips.

Concomitant procedures included CABB in 22, LV cryoaablation in 4, and Maze procedure in 2 patients.

Mitral Leaflet Configuration

The AML and PML tethering angles relative to the line connecting annuli, the posterior and apical displacement of the coaptation, and the IMR grade were measured on echocardiography. Mitral leaflet configuration was quantified in the mid-systolic parasternal long-axis view (Figure 1). AML and PML tethering was measured as the anterior leaflet angle (ALA) and the posterior leaflet angle (PLA), respectively. AML tethering from secondary chordae was measured as the bending angle between tangent lines of proximal and distal AML. Posterior displacement (PD) of the coaptation and the coaptation depth (CD) as apical displacement were measured, respectively. All the patients were evaluated echocardiographically before surgery, 1 month after surgery, and 1 year after surgery.
Subvalvular Apparatus and RMA

Statistical Analysis
All data for continuous variables are expressed as mean±SD. Differences between groups were compared using unpaired t-test and chi-square test. P<0.05 was considered significant.

Results
There was no 30-day in-hospital mortality documented in this series. One month after surgery, residual moderate MR was not detected in either groups, but 2 patients in group 1 developed recurrent moderate MR at 1 year after surgery.

According to mean postoperative LVEF, significant improvement of LV function was seen in each group (group 1, 37.0%±9.2%; group 2, 43.7%±10.5%; NS). And postoperative LV volume data showed that group 2 had significantly smaller LV volume than group 1 (LVESVI/LVEDVI: group 1, 85.3±10.1/118±10.7 ml/m²; group 2, 64.2±10.7/94.4±8.7 ml/m²; P<0.05) at 1 month after surgery. In group 2, the LV volume reduction was achieved by means of combined surgery with CABG, SVR, MAP, PMA, and PMS (Figure 2).

Regarding the mitral valve geometry (Table 2), the PD and the CD from the mitral annulus decreased postoperatively in both groups. Although the preoperative ALA and PLA in group 2 were significantly larger than in group 1, there was significant difference between groups at 1 month after surgery. At 1 year after surgery, however, the situation reversed: the ALA and PLA in group 1 were significantly larger than in group 2 (Figure 3).

Discussion
The presence of MR after myocardial infarction has been associated with a 2-fold increase in mortality with adverse prognosis. Grigioni et al reported that patients with MR after Q-wave myocardial infarction have lower 5-year survival than patients without MR (38±5% vs. 61±6%, P<0.001). Mortality also increases even when the MR is only mild, with an inverse relationship between the severity of MR and survival.

In the setting of IMR, most patients have severe multivessel coronary artery disease and thus often need coronary revascularization using CABG. It is generally accepted that patients with severe IMR who undergo CABG should concomitantly have a surgical procedure to correct MR.

RMA combined with CABG has been the most frequently used technique for the surgical management of severe IMR. Numerous studies, however, have reported a high rate of persistent and/or recurrent MR following RMA with an exponential relationship between the prevalence of postoperative MR and the length of follow-up. Some studies have reported that in the early postoperative phase (<6 months), the prevalence of ≥2+ MR is between 15 and 25%. The prevalence increased markedly after 1 year up to approximately 70% at 5 years.

The results of these studies therefore suggested that the degree of LV impairment rather than MR severity was the main determinant of outcome in the patients with IMR, and
that adding RMA to CABG reduced MR and improved functional outcome in the early postoperative phase but had no or minimal impact on long-term functional and clinical outcomes in these patients.

From a mechanistic point of view, the persistence of MR following RMA has been considered to be related to the persistence or worsening of the tethering of mitral valve leaflets, especially the posterior leaflet. Because the anterior aspect of the mitral annulus is fixed to the aortic root, performing RMA displaces the posterior annulus anteriorly but the posterior leaflet remains tethered posteriorly, changing the valve closure in a single anterior leaflet process. This persistent tethering of the posterior leaflet is considered to be responsible for the residual MR early after RMA in both symmetric and asymmetric tethering patterns.

Several studies identified the preoperative predictors of RMA failure as larger LV diameter, sphericity index, mitral annulus diameter, mitral valve tenting area, and MR severity. One study found that a mitral valve tenting area ≥ 2.5 cm², a coaptation distance ≥ 1 cm and a PLA ≥ 45° measured on TTE have good sensitivity and specificity to predict persistent MR following RMA. This may be explained by the fact that, as opposed to tenting area and coaptation distance, the PLA accurately predicted the persistence of MR in both the symmetric and asymmetric tethering pattern. Moreover, increased preoperative PLA has also been shown to be associated with markedly reduced 3-year event-free survival.

Surgical techniques such as SVR have been considered to help to maintain both a more elliptical ventricle and a higher ejection fraction in patient with ischemic cardiomyopathy. Hvass et al used an encircling loop to approximate the papillary muscles. They noted that their procedure can be helpful in mitral valve closure and in reducing the tethering. Mandegar et al reported early and long-term results on the ventricle shape and function in a group of patients who had undergone PMA in addition to RMA. And Matsui reported on an adjunctive procedure, which has been termed ‘papillary muscle suspension’ (PMS), is considered to prevent future deterioration of tethering by fixing an adequate distance between the mitral annulus and the site of chordal attachment of the papillary muscles. In the present study, we performed PMA and PMS in addition to CABG, MAP, and SVR, because these procedures targeting the mitral valve apparatus and the LV might be beneficial in preventing tethering in the long term.

In this study, we evaluated ALA and PLA using echocardiography before and after surgery. Procedures targeting the subvalvular apparatus including PMA and PMS in addition to MAP (group 2) produced a greater reduction of mitral valve leaflet tethering, compared to group 1 patients. Although the preoperative ALA and PLA in group 2 were significantly larger than in group 1, there was no significant difference between groups at 1 month after surgery. Surprisingly, at 1 year after surgery the situation reversed: the ALA and PLA in group 1 were significantly larger than in group 2. Procedures targeting the subvalvular apparatus including PMA and PMS produced a persistent reduction of mitral valve leaflet tethering at 1 year after surgery, which could not be achieved in patients undergoing CABG and MAP alone. Theoretically, the procedures including SVR, MAP, and PMS in addition to CABG and MAP might be expected to be more effective for preventing the recurrence of mitral leaflet tethering, which might lead to the improvement of long-term outcome.

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