

Long-term effect of papillary muscle approximation combined with ventriculoplasty on left ventricle function in patients with ischemic cardiomyopathy and functional mitral regurgitation[☆]

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Abstract

Objective: One of the mechanisms of development of functional mitral regurgitation after myocardial infarction is the increased papillary muscle distance which results due to ventricle remodeling. The aim of this study was to investigate the long-term effect of papillary muscle approximation (PMA) on the cardiac function of patients with ischemic cardiomyopathy and increased papillary muscle distance. **Methods:** Thirty patients (22 males; mean age: 57.0 ± 7.4 years) selected for coronary artery bypass grafting (CABG) underwent ventriculoplasty. Additionally, 50% of the study population also underwent PMA (group 1). All the patients had preoperative grade 3 or 4 mitral regurgitation with an inter-papillary muscle distance > 2.5 cm. In group 1, the papillary muscles were drawn together using an encircling loop. Mitral annuloplasty and the Dor procedure were performed in all the patients. Follow-up time was 41.5 ± 5.8 months and 42.7 ± 3.3 months in groups 1 and 2, respectively (p -value = 0.49). **Results:** The two groups had no significant difference regarding the annulus diameter, ring size, number of grafts, and concavity area. There was one case of in-hospital mortality in each group, and one patient in group 2 had expired by the last follow-up. Postoperative echocardiography revealed significant changes in the concavity area, ejection fraction, and sphericity index in the PMA group by comparison to group 2 (p -value < 0.05). **Conclusions:** In patients with ischemic mitral regurgitation and increased papillary muscle distance, PMA as an adjunct to CABG results in better left ventricle function and shape, even at long-term follow-up.

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1. Introduction

Functional mitral regurgitation (FMR) in the setting of ischemic cardiomyopathy portends a poor prognosis [1]. After myocardial infarction, the ventricle 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 FMR [2]. Mitral ring annuloplasty is known to be the procedure of choice for FMR; however, as the remodeling of the ventricle continues the chance of recurrence remains high [3,4] if the subvalvular structure is not addressed at the time of coronary artery bypass grafting (CABG). Surgical techniques such as ventricle restoration operations help to maintain both a more elliptical ventricle and a higher ejection fraction in patient with ischemic cardiomyopathy.

Yu et al. [5] reported that the increased interpapillary muscle distance to be associated with FMR. Hvas et al. [6] used an encircling loop to approximate the papillary muscles they stated that their procedure can be helpful in mitral valve closure and reducing the tethering. In our previous study, we reported early results on the ventricle shape and function in a group of patients with a papillary muscle distance more than 2.5 cm and ischemic cardiomyopathy, who had undergone papillary muscle approximation in addition to ring annuloplasty [7]. The present study aims to report the long-term result of the same group of patients and to compare them with the group who had not undergone papillary muscle approximation.

2. Methods

2.1. Patient population

Between October 2004 and June 2005, 30 patients (22 men and 8 women) with ischemic cardiomyopathy at Day General Hospital were enrolled in this study. All the patients were

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selected based on increased interpapillary muscle distance, restricted leaflet motion, concave anterior leaflet, and otherwise structurally normal valve and varying degrees of annular dilation in combination with reduced ventricular ejection fraction with scar tissue formation in the apex observed by preoperative and intra-operative echocardiography. Our policy was to repair the mitral valve if the patients had symptomatic MR, grade III–IV FMR, and large left ventricular (LV) volume. All the selected patients had an interpapillary muscle distance of more than 2.5 cm. The mean preoperative ejection fraction was $23 \pm 6\%$. The LVEDV was 278 ± 54 ml and all patients had New York Heart Association Class (NYHA) III–IV. Written consent was obtained from all the patients and the study protocol was approved by our Institutional Ethics Committee on Human Study.

2.2. Echocardiography

All patients underwent preoperative and intra-operative echocardiography. The mitral valve was assessed by the concavity area and the MR grade was determined quantitatively with calculation of effective regurgitant orifice area, regurgitant fraction, and regurgitant volume by PISA method.

Concavity area was used to evaluate the mitral valve condition.

In order to measure the interpapillary muscle distance, the parasternal short-axis view on TTE and transgastric view on TEE was used.

LF sphericity index calculated as the ratio of LF internal diameter in short-axis view compared to LF length (measured as the distance from mitral annulus to apical endocardium in LF long-axis view).

2.3. Technique

All patients underwent complete revascularization and LV reconstruction according to Dor procedure. In group 1, pericardial ring annuloplasty was performed and the papillary muscles were approximated. In group 2, pericardial ring annuloplasty alone was performed.

After a median sternotomy, moderate hypothermic cardiopulmonary bypass was performed through aortic and caval cannulation. Both antegrade and retrograde cold-blood cardioplegia were used for myocardial protection. Once the mitral valve was exposed through a superior septal incision, the valves were inspected and the pathophysiology was confirmed. Several 3/0 braided polyester sutures in the posterior annulus were used to bring the mitral valve closer to the operative field, which were later utilized for annuloplasty ring placement. The free edge of the anterior leaflet was used for the selection of the ring size. The left ventricle was opened from the center of scar and the scar was resected. If the infarction was anteroapical or septal, the incision was made parallel to the left anterior descending artery (surgical anterior ventricular endocardial restoration (SAVER) procedure) [8]. The increased papillary muscle distance was observed in all the patients enrolled in the study; in group 1, a 4-mm Gore-Tex tube or umbilical tape was used to draw the papillary muscles together (Fig. 1). All patients underwent full revascularization and endoventricular circular patch plasty (Dor). To cinch the scar area and to

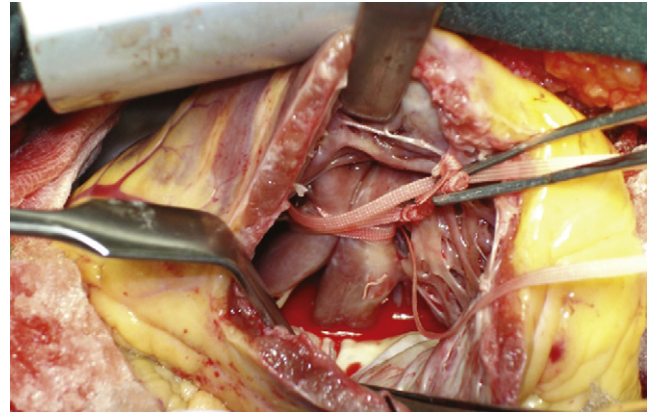


Fig. 1. The papillary muscles were drawn together with a 4 mm Gore-Tex tube or umbilical tape.

obtain a normal internal ventricle outline, a 2 to 0-monofilament suture was used to encircle the fibrous tissue and, as a result, an orifice was constructed that excluded the scar zone and became the base for patch insertion. For closing the orifice and reconstructing the left ventricle, a circular Dacron patch was anchored to the fibrotic tissue. Finally, to have a better hemostasis and by reinforcing the suture lines the excluded fibrotic tissue was folded over the patch.

After weaning from the cardiopulmonary bypass, in all patients intra-operative transesophageal echocardiography was performed and the LV shape and mitral valve function were assessed. All patients also were evaluated at 1 month and then every 3 months for the first year. Thereafter, the patients were followed up by history, physical examination, and transthoracic echocardiography annually.

2.4. Statistical analysis

The numerical values were expressed as mean and standard deviation (SD). The data were compared between the two groups using the unpaired *t*-test for the continuous variables and Fisher's exact test for sex. Longitudinal changes in the parameters were compared between the two groups by general linear model repeated-measurement analysis of variance (ANOVA).

All the statistical analyses were performed using the SPSS Version 16.0 program. A *p*-value < 0.05 was considered statistically significant.

3. Results

Residual MR was acceptable in all patients. After weaning, the patients from the cardiopulmonary bypass five patients required intra-aortic balloon pump (IABP). Most cases required medical inotropic support with noradrenaline and milrinone. In the hospital, one patient died in the PMA group due to uncontrollable ventricular arrhythmia and one in the non-PMA group due to pump failure. By the last follow-up three patients died.

The patients' baseline characteristics were reviewed (Table 1) and it was observed that there were no significant

Table 1. The comparison of patient characteristics and background in the two groups.

	PMA	Non PMA	p-Value
Age	57.0 ± 8.0	58.5 ± 9.3	0.65
Sex (male/female)	10/5	12/3	0.68
PMD	2.99 ± 0.27	2.84 ± 0.29	0.15
Number of grafts	3.5 ± 1.1	3.7 ± 1.7	0.61
% Mortality	7	13	1
Follow-up time	41.5 ± 5.8	42.7 ± 3.3	0.49
Ring	27.9 ± 1.4	27.7 ± 1.3	0.79

differences between the two groups regarding the baseline characteristics (p -value > 0.05).

LVEDV, LVESV, and LVESVI were smaller in the PMA group by the last follow-up; however, the difference between the two groups was not statistically significant (p -value > 0.05). Both groups showed improvement in the ejection fraction, which was 36 ± 6.1 in the PMA group and 29.3 ± 5.8 in the non-PMA group by the last follow-up. The difference between the two group was significant regarding their ejection fraction ($p = 0.048$).

The concavity area of the anterior leaflet showed significant change in the PMA group from 44.0 ± 4.2 to 8.3 ± 1.3 by the last follow-up; this change was less significant in the control group changing from 45.9 ± 4.2 to 29.3 ± 5.8 . Systolic sphericity index changed from 65.1 ± 3.4 to 55.8 ± 3.3 and diastolic sphericity index from 48.1 ± 4.5 to 38.1 ± 5.1 in the PMA group; however, the changes in the sphericity indices were not significant in the non-PMA group (Table 2). The non-PMA group also showed significant more residual MR (mean MR grade = 2.31 ± 1.03) compared with the PMA group (mean = 0.85 ± 0.90) by the last follow-up which showed significant difference between the two groups (p -value = 0.001).

4. Discussion

After myocardial infarction, the left ventricle undergoes remodeling and becomes more spherical; this contributes to papillary muscle lateral displacement and development of FMR and the resultant low ejection fraction. Restoring the elliptical shape of LV and preventing its expansion have been shown to improve the ejection fraction and reduce the severity of FMR in patients with severely dilated ventricle [9,10].

Although using undersized mitral annuloplasty rings looked promising by improving ejection fraction and NYHA class [11], there were still reports of recurrences of about 20–50% within a few years and, as a result, several techniques have been since introduced which addresses the papillary muscle tethering or displacement [6,12–15] or the ventricle dilatation and sphericity [12–14]. However, most of these procedures find to be complex and time consuming.

One of the proposed mechanisms of recurrence is the papillary muscle tethering and displacement which can restrict leaflet motility and derange the normal chordal leaflet alignment. Papillary muscle distance has been shown to be important in the development of FMR and its recurrence [16,17]. Jorapur et al. [17] showed a difference between papillary muscle distance in normal patients, those with dilated cardiomyopathy and FMR, and patients with dilated cardiomyopathy without FMR. In the normal group, the separation was 1.49 ± 0.24 in those with FMR 2.91 ± 0.3 cm and in those without FMR the separation was 2.02 ± 0.36 ; in their study, it was observed that the severity of MR correlated with papillary muscle distance. In another study based on cine magnetic resonance imaging findings, it was demonstrated that as coronary artery disease develops the end systolic volume increases which consequently affects the interpapil-

Table 2. The comparison of echocardiography measure between the two groups.

Variables	Groups	Before operation	1st Follow-up	Last follow-up	p-Value
MR	PMA	3.53 ± 0.52	0.57 ± 0.76	0.85 ± 0.90	0.001
	Non PMA	3.33 ± 0.49	1.50 ± 0.86	2.31 ± 1.03	
LVESV	PMA	177.1 ± 7.5	81.0 ± 13.5	84.5 ± 13.1	0.12
	Non PMA	168.7 ± 9.1	90.6 ± 6.6	95.4 ± 6.7	
LVESVI (ml/m ²)	PMA	97 ± 8.8	47.6 ± 8.6	47.9 ± 8.3	0.3
	Non PMA	94.4 ± 8.6	51.1 ± 4.1	53.1 ± 3.9	
LVEDV	PMA	283.9 ± 16.1	171.0 ± 17.2	170.7 ± 17.4	0.17
	Non PMA	271.3 ± 26.3	183.7 ± 14.7	191.8 ± 20.7	
EF (%)	PMA	23.0 ± 2.9	36.0 ± 6.6	36.0 ± 6.1	0.048
	Non PMA	23.5 ± 3.3	32.9 ± 5.1	29.6 ± 5.6	
Con a (mm ²)	PMA	44.0 ± 4.2	8.0 ± 1.9	8.3 ± 1.3	0
	Non PMA	45.9 ± 4.2	24.0 ± 4.7	29.3 ± 5.8	
Sys Sph	PMA	65.1 ± 3.4	55.0 ± 3.5	55.8 ± 3.3	0
	Non PMA	67.0 ± 3.5	63.4 ± 4.7	69.3 ± 5.3	
Dia Sph	PMA	48.1 ± 5.7	37.9 ± 4.7	38.1 ± 5.1	0
	Non PMA	47.5 ± 4.5	51.4 ± 4.5	54.4 ± 3.5	
AnnulusDia	PMA	3.94 ± 0.25	2.79 ± 0.23	2.79 ± 0.22	0.65
	Non PMA	3.88 ± 0.20	2.76 ± 0.26	2.78 ± 0.25	

MR, mitral regurgitation; LVESV, left ventricle end-systolic volume; LVEDV, left ventricle end-diastolic volume; EF, ejection fraction; Con a, concavity area; Sys Sph, systolic sphericity; Dia Sph, diastolic sphericity; Annulus Dia, annulus diameter.

lary distance; it was stated that a papillary muscle distance more than 3.2 cm was associated with the presence of FMR [5]. In a previous study, we documented a mean inter group [16].

The correction of papillary muscle distance with different techniques has been reported; in the study by Isomura et al. [18] papillary muscles were approximated by two sutures after the ventricle muscle between the papillary muscles were resected. We used another technique with a sling and preferred to respect the papillary muscle with the no-touch technique. Matsui et al. [19] used the papillary muscle approximation in a group of patients with dilated cardiomyopathy, which showed favorable results on the tethering of the mitral valve. Rama et al. [20,21] reported a technique of papillary muscle approximation using a 2/0 U-shaped stitch reinforced by pericardial patch in a group of eight patients with ischemic MR and LV dysfunction with good early results, although their long-term outcome remains to be reported. Hvass and Joudinaud [22], in a recent study, reported their results of PMA in a group of 37 patients with severe ischemic FMR, the mean follow-up in their study was 55 ± 22 months and the regurgitation was none to trivial in 31 patients and mild to moderate in four; in their study adverse remodeling was expected in.

In our previous study, it was demonstrated that papillary muscle approximation in the selected patients can have effect on the sphericity index reducing systolic and diastolic sphericity indices from 65.1 ± 3.4 and 48.1 ± 5.7 to 55.0 ± 3.5 and 37.9 ± 4.7 and restoring the LV shape to more elliptical form by the 9 month [7]. During the follow-up period, the PMA group also maintained the improvement in sphericity indices showing a systolic and diastolic sphericity indices of 55.8 ± 3.3 and 38.1 ± 5.1 , respectively. In addition, Dor operation was performed in this study as most of our patients had apical aneurysm and a more linear approach, which results in a more conical-shaped ventricle, was not possible; the Dor procedure results in a wider ventricle wall dimension and PMA helps to restore a more elliptical-shaped ventricle and partially corrects the malstructure.

In our experience, papillary muscle approximation is a safe and easy technique to perform in high-risk patients, which can avoid using an undersized ring and contributes to a more normal aligned subvalvular apparatus. Addressing the subvalvular apparatus has paramount importance in preventing the recurrence of ischemic MR; adding the papillary muscle approximation will result in a smaller mid-ventricle diameter, a more elliptical left ventricle, and reduces the tension on the annulus preventing its progressive dilatation. In our group of patients, this resulted in a significant difference in the recurrence of IMR at long-term follow-up, with better ejection in the PMA group.

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Appendix A. Conference discussion

Dr R. Fuster (Valencia, Spain): This long-term study updates a previous report. Functional MR is a difficult situation which occurs as a consequence of regional or global left ventricular dysfunction despite a structurally normal valve and it is a common and relevant complication in these patients with

ischemic cardiomyopathy, because its presence increases long-term mortality even after surgical valve repair.

So, in my opinion, the key point in treating these patients is the understanding of a complex pathophysiology that is usually a combination of several geometric and hemodynamic factors: number one, the mitral valve annulus; number two, the tethering of the leaflets by the displaced papillary muscles; and number three, the left ventricular dysfunction and remodeling. But this is not a static scenario. We must fight against a complex enemy, a dynamic process of post-infarction left ventricular remodeling.

Therefore I think the surgical technique must be aggressive, must be focused on this complex pathophysiology addressing three points. Of course, number one, the mitral valve annulus with an aggressive annuloplasty with undersizing. Secondly, mitral valve apparatus with several techniques (I think we can use this technique for approximation or apposition of papillary muscles). Number three, the left ventricle, and I think it is very important to assess the myocardial viability in these patients and also study left ventricular geometry and function. So we must select the best technique to cover these three points.

According to this, I have these questions. Number one, mitral valve annuloplasty with a prosthetic ring and an aggressive undersizing, and even with the use of special rings such as GeoForm, should be highly recommended in these patients to compensate mitral valve tethering. Don't you agree that patients from group 2 without approximation of papillary muscles would have had a significant improvement of their outcomes with an aggressive annuloplasty with undersizing with the use of a prosthetic ring? In the manuscript you refer to pericardial annuloplasty. What type of annuloplasty have you used in these patients?

And another question. How can you adjust your correction? How much do you approximate both papillary muscles in order to achieve an optimal result avoiding under-correction or over-correction? And have you used an intraventricular balloon?

And finally, we must restore several things in these patients, left ventricular mitral valve geometry and function, and, above all, we must also restore myocardial perfusion by means of CABG. So I think we need important information about the number and the location of nonviable segments in the three coronary territories. Have you used MRI or other type of study to assess the location and number of nonviable segments?

Dr Roshanali: In reply to the first question, yes, we indeed used pericardial rings in this series, after which we used prosthetic rings. I should emphasize that in this series of patients, we used complete pericardial rings. That means we put the sizer on the pericardium and tailored the complete pericardium in order to shape it into a prosthetic ring. However, we know that it is not now recommended for functional MR and that we should therefore use non-flexible rings.

And as for the second question, we over-corrected the papillary muscles. We adjusted them until they were completely together.

Regarding the third question, we performed stress echocardiography in all the patients, all of whom had acceptable myocardial viability for operation.

Dr R.U. Nair (Leeds, UK): In 1998 we described papillary muscle plication as an alternative to the Batista operation and in 2001 published our first series of nine patients including one patient who had been listed for transplantation because of very high pulmonary artery pressure. Since then we have published a series of 30 patients with a follow-up up to 2005, and that was published in 2008. We compared these patients with a matched group of CABG patients and found consistent improvement in the functional reserve of the myocardium.

The question I want to ask you is how many sutures do you normally use to approximate the papillary muscles?

Dr Roshanali: In this group of patients we did not use any sutures. In some of our other patients (not this group), we have used sutures with pledgets on fragile papillary muscles. But let me emphasize that, in this series, we only used umbilical tape or a Gore-Tex tube and did not make use of sutures.

I should also mention that we benefited enormously from your paper, for which I owe you a big thank you!

Dr S. Bolling (Ann Arbor, MI): Your mean interpapillary muscle distance in both groups is about 2.8 or 2.9, which is not extremely dilated. Some of the interpapillary muscle distances that we have seen have been 3 or 4 or 5 cm. Have you done this technique in much larger hearts?

Dr Roshanali: I have never seen a papillary muscle distance size larger than 4 cm up to now in my echocardiography practice, and certainly not in the operating room. In the operating room you might see a distance more than 6 cm. However, a distance in excess of 2 cm in end-systole in echocardiography is regarded as high.