Mid-term results of papillary muscles approximation

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Background Adjunctive subvalvular repair during mitral annuloplasty for secondary mitral regurgitation is effective in preventing recurrent regurgitation. One of these procedures is papillary muscle approximation. However, the safety and the positive impact of this method are still open to question.

Aim This study focused on the assessment of mid-term results of papillary muscles approximation and comparison of the obtained results with those of isolated mitral annuloplasty.

Methods Two hundred and twelve patients with ischemic cardiomyopathy and ischemic mitral regurgitation were enrolled in this retrospective single-center study. The patients were randomised to 2 groups by using propensity score matching (a "neighbor" method) according to the following parameters: end diastolic volume, end systolic volume, stroke volume and ejection fraction. The first group included 112 patients with ischemic cardiomyopathy and mitral regurgitation, who underwent coronary artery bypass grafting, mitral annuloplasty and papillary muscle approximation. The second group included 112 patients with ischemic cardiomyopathy who underwent coronary artery bypass grafting and mitral valve annuloplasty. We evaluated early and mid-term results.

Results Two patients in group 1 and three patients in group 2 died of heart failure progression during 31.3±10.4 month follow-up. According to the Kaplan-Meier analysis, no statistically significant differences were noted between the groups (log-rank test = 0.8). Approximation of papillary muscles in patients with ischemic mitral regurgitation improved mitral valve leaflet coaptation as evidenced by the values of coaptation depth, coaptation line and tenting area ($p>0.05$). During follow-up, 3 cases (2.7%) of mitral insufficiency recurrence were recorded in group 1 and 16 (14.3%) in group 2. The Kaplan-Meier analysis of cumulative probability showed a significant difference in freedom from recurrence of mitral regurgitation ≥2 between groups in the mid-term postoperative period (log-rank test = 0.041).

Conclusion Adjunctive papillary muscle approximation performed at the time of mitral annuloplasty improves the durability of mitral valve repair.

Keywords mitral valve repair; papillary muscle approximation

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Introduction

Ischemic mitral regurgitation (IMR) is diagnosed in 10–50% of patients after myocardial infarction [1]. Among several surgical procedures, mitral ring annuloplasty has been the method of choice for an appreciable length of time. However postoperative recurrence of mitral regurgitation ranges from 5 to 58% [2–4]. Studying the mechanisms underlying MR recurrence after annuloplasty might explain these unsatisfactory outcomes. The pathophysiology of IMR is complex and results from an imbalance between closing and tethering forces acting on the mitral valve (MV). Enlargement of the left ventricular (LV) and displacement of papillary muscles in the apical and lateral directions increase the tethering forces. Left ventricular and papillary muscle dyssynchrony and reduced myocardial contractility curtail the closing forces, thus leading to impaired leaflet coaptation and appearance of MR [8]. Therefore, treatment of mitral insufficiency requires an integrated approach, affecting all aspects of the pathogenesis of MR recurrence.

Recent publications show that adjunctive subvalvular repair during mitral annuloplasty for secondary mitral regurgitation is effective in preventing recurrent regurgitation. One of such procedures is papillary muscle approximation. However, the safety and positive impact of this method are still open to question.

The aim of the study to evaluate the mid-term results of papillary muscles approximation as a supplement to conventional procedure of ischemic mitral regurgitation treatment.

Methods

Penza Federal Cardiovascular Surgery Center's surgeons (Penza, Russian Federation) performed 430 operations including mitral annuloplasty and coronary artery bypass grafting, as well as 112 operations comprising coronary artery bypass grafting , mitral valve

Table 1. Baseline patients' characteristics before Propensity Score Matching

Indicator		Group 1, n = 112	Group 2, n = 430	p
Clinical and demographic characteristics				
Age (years)		59.7±6.1	60.75±6.8	0.26
Males		103 (92)	349 (81)	0.001
Body mass index (kg/m^2)		29.3±4.21	29.1±3.5	0.7
Body surface area (m^2)		2.1±0.15	2.07±0.13	0.11
Hypertension		36 (32)	117 (27)	0.3
Diabetes mellitus		27 (24)	105 (24)	0.95
Obesity		5 (4.5)	5 (1.1)	0.02
Chronic obstructive pulmonary disease		5 (4.5)	7 (1.6)	0.07
Multifocal atherosclerosis		22 (20)	69 (16)	0.36
III/IV NYHA class		26 (23)	35 (8)	0.001
EuroSCORE		5.36±2.1	6.0±2.83	0.06
6MWT		333±65	340±69	0.43
Echocardiographic characteristics				
End-diastolic volume (ml)		189,9±51,1	167±43,7	0,12
End-systolic volume (ml)		124,6±47,8	93,7±38,1	0,005
Stroke volume (ml)		65,3±12,3	73,3±18,7	0,001
Ejection fraction (%)		36,3±9,66	45,5±11,4	0,041
Mitral regurgitation	mild	49 (33)	221 (51)	
	moderate	18 (16)	96 (22)	
	severe	45 (51)	113 (26)	

Data presented as n (%) or mean (M) ± standard deviation (SD). *NYHA*, New York Heart Association; 6MWT, six minute walking test

annuloplasty and papillary muscle approximation. Patients with mitral valve damage, unstable angina or with a recent experience of myocardial infarction (less than 6 months), or serious dysfunction of the right ventricle, papillary muscle rupture, multi organ failure, concomitant reconstruction of the left ventricle, interventions on the aortic valve were excluded. Patients' baseline characteristics are presented in Table 1.

The analysis revealed a statistically significant difference between patients of both groups in such parameters as end-systolic volume (ESV), stroke volume (SV) and ejection fraction (EF). Propensity Score Matching was performed and patients were compared by end-diastolic volume (EDV), ESV, SV, EF and age. The control group included 112 patients. The clinical/demographic characteristics and echocardiographic data of the patients are given in Table 2.

Propensity Score Matching results showed that the patients' clinical and echocardiographic characteristics in both groups were comparable. To assess the efficacy of papillary muscle approximation to be added to a conventional technique for IMR treatment, geometrical and functional parameters of the left ventricle were chosen as primary endpoints. All

Table 2. Patients' preoperative characteristics

Indicator		Group 1, n = 112	Group 2, n = 430	p
Clinical and demographic characteristics				
Age (years)		59,7±6,1	59,21±6,36	0,55
Males		103 (92)	94 (84)	0,06
Body mass index (kg/m2)		29,32±4,21	29,1±3,5	0,67
Body surface area (m2)		2,1±0,15	2,08±0,13	0,32
Hypertension		36 (32)	26 (23)	0,14
Diabetes mellitus		27 (24)	26 (23)	0,88
Obesity		5 (4,5)	5 (4,5)	1
Chronic obstructive pulmonary disease		5 (4,5)	5 (4,5)	1
Multifocal atherosclerosis		22 (20)	20 (18)	0,73
III/IV NYHA class		26 (23)	18 (56,3)	0,18
EuroSCORE		5,36±2,1	5,82±2,55	0,14
6MWT		333±65	339,25±69,3	0,5
Echocardiographic characteristics				
End-diastolic volume (ml)		189,9±51,1	185,4±45,1	0,36
End-systolic volume (ml)		124,6±47,8	120,1±40,3	0,11
Stroke volume (ml)		65,3±12,3	64,8±14,6	0,41
Ejection fraction (%)		36,3±9,66	36,3±9,4	0,67
Interpapillary muscle distance in systole (mm)		32±9,8	31,3±7,9	0,56
Interpapillary muscle distance in diastole (mm)		39,1±8,5	38,9±7,4	0,85
Mitral regurgitation	mild	49 (33)	42 (37,5)	
	moderate	18 (16)	31 (28)	
	severe	45 (51)	39 (34,5)	
Fibrous ring size (mm)		42,4±4,1	41,9±3,8	0,17
Coaptation depth (mm)		8,6±1,5	8,3±1,8	0,09
Coaptation line (mm)		1,8±0,7	1,9±0,6	0,13
Tethering area (mm^2)		4,4±0,7	4,35±0,7	0,3

Data presented as n (%) or mean (M) ± standard deviation (SD). *NYHA*, New York Heart Association; *6MWT*, six minute walking test

patients had undergone transthoracic echocardiography preoperatively. The results were confirmed by means of intraoperative transesophageal echocardiography performed after general anesthesia induction and prior to surgical incision. Variables with a prognostic value for MR recurrence (EF, MR degree, EDV, ESV, length and line of coaptation, distance between papillary muscles in systole and diastole) were recorded for each patient.

Propensity Score Matching results showed that the patients' clinical and echocardiographic characteristics in both groups were comparable. To assess the efficacy of papillary muscle approximation to be added to a conventional technique for IMR treatment, geometrical and functional parameters of the left ventricle were chosen as primary endpoints. All patients had undergone transthoracic echocardiography preoperatively. The results were confirmed by means of intraoperative transesophageal echocardiography performed after general anesthesia induction and prior to surgical incision. Variables with a prognostic value for MR recurrence (EF, MR degree, EDV, ESV, length and line of coaptation, distance between papillary muscles in systole and diastole) were recorded for each patient.

Echocardiography protocol

The following parameters were measured:

• LV volumes (EDV, ESV), EF were evaluated by Simpson's upgraded test.

• Depth of coaptation was measured as a distance between the ring surface and the matching point of leaflets using an apical four-chamber view.

• Tethering area is a space restricted by the annulus plane and mitral leaflets.

• Interpapillary distance was measured in a parasternal position alongside a short cardiac axis when using transthoracic examination or as a distance between papillary muscles during transesophageal echocardiography.

• Size of the mitral valve ring was measured from apical two- and four-chamber view as a distance from the base of posterior and anterior leaflets.

Mitral insufficiency was assessed according to American Society of Echocardiography guidelines. Vena contracta (VC) was measured as the narrowest point for the regurgitation jet by using a color Doppler.

Regurgitation volume (RV) was defined as regurgitation volume = mitral regurgitation volume/stroke volume. Severity of mitral insufficiency was classified as follows:

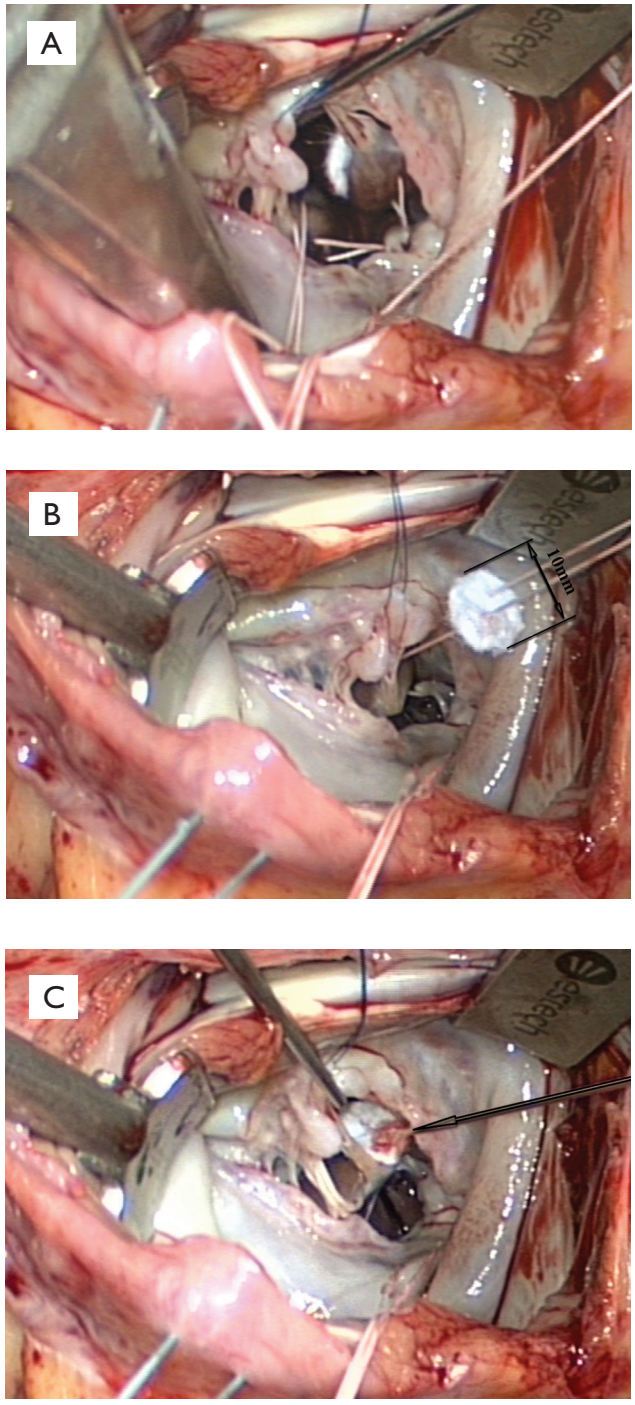

Fig. 1. Stages of papillary muscle approximation: muscle heads brought together (*A*); PTFE gasket prior to pulling through in the left ventricular cavity (*B*); the gasket is fixed with a tightly ligated knot; papillary muscles are approximated (*C*)

mild VC<3 mm, RV<30%; moderate VC = 3–6 mm, RV = 30–50%; severe VC>6 mm, RV>50%.

Control echocardiography was carried out at hospital discharge, after 6 months and then annually during outpatient examinations.

Surgery

Mitral valve plasty was initiated in the case of severe mitral insufficiency confirmed by transthoracic echocardiography, or in the case of mild mitral insufficiency, with MV fibrous annulus exceeding 40 mm. Papillary muscle approximation was indicated if only interpapillary distance exceeded 35 mm in diastole and 25 mm in systole. All operations were done by one surgical team. In all cases, median sternotomy was used. Operations were performed under normothermic perfusion, aortal and bicaval cannulation, with the use of cardioplegic solution Custodiol®.

In most cases, coronary artery bypass grafting was performed by using internal thoracic arteries. If the latter were damaged or not available, we used a vein graft. Left internal artery was used for shunting the anterior descending artery in the case of isolated damage. In patients with 2 or 3 damaged vessels, coronary artery bypass grafting was performed by means of composite T-grafts. Following the coronary stage, MV was approached through the interventricular septum. Visual examination of MV enabled us to exclude the pathologies of leaflets, papillary muscles and chords. Papillary muscles were approximated via MV fibrous annulus at the level of heads (Fig. 1). To this end, we used nonabsorbable braided suture 2.0 (Ethibond, Ethicon, Inc.) and felt gaskets.

"MedIng" (Penza, Russian Federation) backup rings sized from 28 to 30 mm were used for mitral annuloplasty. The rings were secured by using special U-shaped seams with Ethibond 2-0 suture (Ethicon, Inc., USA). Annuloplasty over, the LV cavity was filled up with a saline solution

Table 3. Patients' intraoperative and early postoperative characteristics of both groups

Variable		Group 1, n = 112	Group 2, n = 112	p
Cardiopulmonary bypass (min)		141,8±48,6	149,9±52,4	0,23
Myocardial infarction (min)		90,1±25,2	94,2±28,9	27
Distal anastomosis (n)		2,4±0,9	2,31±1	0,48
Ventilatory support (hr)		5,13±4,2	5,3±4,5	0,77
Length of stay at ICU (days)		2,8±2	3±2,72	0,53
Inpatient stay (days)				
End-diastolic volume (ml)		177,4±37,9	180±45,6	0,59
End-systolic volume (ml)		112,1±35,4	117,8±41	0,33
Stroke volume (ml)		65,2±11,4	62,5±9,7	0,83
Ejection fraction (%)		38,88±6,69	35,1±8,3	0,003
Interpapillary muscle distance in systole (mm)		24±12,1	29,3±6,8	0,001
Interpapillary muscle distance in diastole (mm)		31,4±14	37±7,1	0,002
Mitral regurgitation (%)	0	106	101	0,21
	mild	6	11	0,21
Backup ring size (mm)		29,3±1,14	29,6±1,4	0,08
Mean gradient		2,5±0,8	2,4±0,81	0,35
Maximum gradient		4,9±1,6	5,4±1,8	0,03
Coaptation depth (mm)		5,4±2,8	6,71±1,45	0,001
Coaptation line (mm)		4,6±1,35	4±1,3	0,001
Tethering area		2±0,41	3±0,51	0,001

Data presented as n (%) or mean (M) ± standard deviation (SD). *ICU*, intensive care unit

to assess the efficacy of plasty. Hydraulic tests were satisfactory in all cases.

Statistical analysis

Software packages SPSS Version 21 (IBM Corp., Armonk, USA) were used to statistically process the data obtained. To compare the results between groups, an arithmetic mean value ($M = \sum / n$), a standard deviation from the general population (s), was calculated. Data presented as n (%) or mean (M) ± standard deviation (SD). Categorically expressed data were compared by means of the $\chi 2$ test. A critical significance level was taken as 0.05. A cumulative risk of MR recurrence during long-term follow-up was evaluated using Kaplan-Meier test.

Results

Control echocardiography was carried out intraoperatively, after cardiopulmonary bypass termination, also after inpatient care. On average, this period ran to 11±5.5 days. Patients' intraoperative and early postoperative characteristics of both groups are given in Table 3.

Cardiopulmonary bypass and myocardial ischemia time in both groups were comparable. Thus, additional approximation of papillary muscles does not significantly augment surgery timing. Early follow-up resulted in no complications, which was confirmed by pulmonary support time and length of ICU/hospital stay.

We observed improved LV/MV configurations by the following parameters: ejection fraction, coaptation height and line, tethering area, maximum gradient, interpapillary muscle distance in systole and diastole ($p>0.05$). All patients underwent medical examination, transesophageal echocardiography and a 6 minute walking test. Follow-up amounted to 31.3±10.4 months. Table 4 provides mid-term follow-up outcomes.

In this period two patients from group 1 and three patients from group 2 died. According to Kaplan-Meier analysis, no statistically significant differences were recorded between groups (log-rank test = 0.8). Approximation of papillary muscles in patients with ischemic mitral regurgitation improved MV leaflet coaptation, which was confirmed by the values of coaptation depth and line, as well as the tethering area ($p>0.05$).

During the follow-up, 3 cases (2.7%) of mitral insufficiency recurrence in group 1 and 16 cases (14.3%) in group 2 were observed. We analyzed an overall risk of

Table 4. Mid-term follow-up outcomes

Variable		Group 1, n = 112	Group 2, n = 112	p
End-diastolic volume (ml)		177,4±37,9	180±45,6	0,59
End-systolic volume (ml)		112,1±35,4	117,8±41	0,33
Stroke volume (ml)		65,2±11,4	62,5±9,7	0,83
Ejection fraction (%)		38,88±6,69	35,1±8,3	0,003
Interpapillary muscle distance in systole (mm)		24±12,1	29,3±6,8	0,001
Interpapillary muscle distance in diastole (mm)		31,4±14	37±7,1	0,002
Mitral regurgitation (%)	0	97	77	
	mild	12	17	
	moderate	3	14	
	severe	–	2	
Mean gradient		3,35±1,7	4,51±2,3	0,001
Maximum gradient		9,1±3,4	10,5±5,7	0,03
Coaptation depth (mm)		5,3±2,3	8±2,2	0,001
Coaptation line (mm)		4,9±1	3,6±1,1	0,001
Tethering area		2,1±0,5	3,3±0,6	0,001
6MWT		407±85	381±52	0,01

Data presented as n (%) or mean (M) ± standard deviation (SD). *6MWT*, six minute walking test

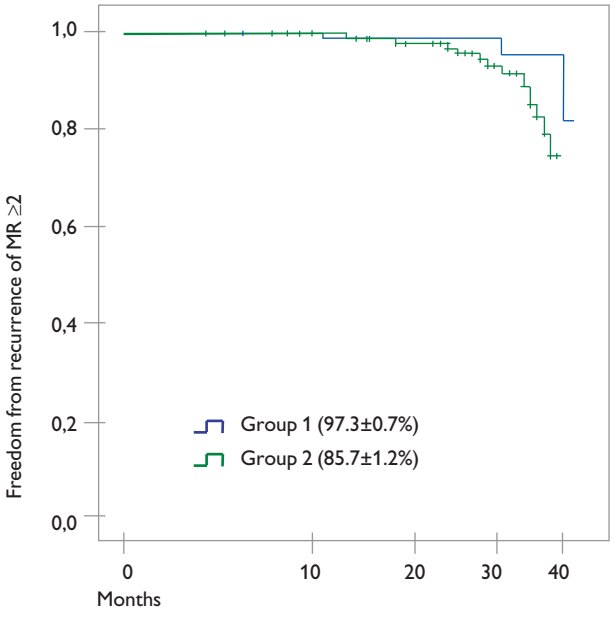

Fig. 2. Freedom from recurrence of moderate and acute mitral regurgitation (MR) (Kaplan-Meier analysis)

moderate and severe MR recurrences in patients of both groups within the 31.3±10.4-month follow-up. Kaplan-Meier analysis demonstrated a statistically significant difference in the frequency of moderate and severe MR between groups in the mid-term follow-up (Fig. 2).

Multivariate regression analysis revealed that ejection fraction reduction down to 30% and less leads to an increase of MR recurrence by 39 times, while the use of isolated annuloplasty increases the recurrence by 14.36 times (Table 5).

Discussion

At the close of the 20th century, there started a lively discussion of the etiology of ischemic mitral insufficiency. Some authors claimed that MR recurrence is caused only by papillary dysfunction and ischemic cardiomyopathy progression, which lead to incomplete leaflet coaptation. Others thought that dilatation of LV cavity and its volume overload result in the enlargement of MV fibrous annulus, thus triggering MR recurrence. The third group of researchers suggested that not only the structural-functional mechanism but the geometric components, particularly the distance from papillary muscles base to the plane of MV annulus, play an important role in this recurrence. It is the increased depth of coaptation that finally leads to MR relapse. Introducing new visualization methods in clinical practice allowed for combining all theories of ischemic MR development into one. Hence, ischemic myocardial changes lead to an enlarged cavity of the left ventricle and, as a consequence, to apical and lateral displacement of the subvalvular apparatus. The displacement of papillary muscles causes tension of MV chords and reduced coaptation of the leaflets. Besides, LV dilatation provokes an increase of MV annulus, which also contributes to a shortening of the leaflet coaptation line [17, 18].

The foregoing shows that surgeons are supposed to solve two problems during repair of ischemic mitral regurgitation:

1. Reducing the size of the fibrous annulus which should increase the coaptation area of MV leaflets (mitral annuloplasty).

Table 5. Multivariate regression analysis

Variable	Hazard ratio	95% Confidence interval	p
Posterior Q-MI	1.39	0,3–6,38	0,67
Anterior Q-MI	3.74	0,38–36,74	0,26
End-diastolic volume ≥220 ml	2.45	0,15–39,72	0,53
Ejection fraction ≤30%	39.02	3,65–416,8	0,002
Isolated annuloplasty	14.36	19,0–105,8	0,009

MI, myocardial infarction

2. Shortening the distance between papillary muscles and, consequently, reducing the tension between the base of papillary muscles and the mitral annulus plane, which also increases the area of leaflet coaptation (papillary muscle approximation).

Until a certain period, mitral annuloplasty was chosen as a strategy for surgical management of ischemic mitral insufficiency, where just one of the problems was solved, namely, removal of fibrous annulus dilatation. However, recent research data point to a high incidence of MR recurrence when using this procedure, from 10 to 37% [19–23].

In 2002, I.L. Kron et al. described a technique for transposition of posterior papillary muscle demonstrating that this procedure contributed to restoration of a physiological configuration of the mitral leaflets without MR recurrence during early follow-up [24]. In 2003, U. Hvass et al. proposed a method of approximating anterior-medial and posterior-lateral groups of papillary muscles in combination with mitral annuloplasty. This study showed that the given procedure can be used in patients with ischemic MR, as long as it improves the geometry of MV leaflets [25].

In 2007, A. Rama et al. reported that approximation of papillary muscles reduces the incidence of MR recurrences, inhibits LV remodeling and downgrades NYHA functional class [26].

In 2008, S. Ishikawa et al. described a "sandwich-plasty" technique involving approximation of uniform groups of papillary muscles in combination with MV annuloplasty (the authors used a Carpentier-Edwards Physio Ring). This research also showed a positive effect of the procedure on MV geometry in patients with ischemic mitral regurgitation [27].

Subsequent researches confirmed the fact that mitral annuloplasty combined with papillary muscle approximation is more effective than isolated mitral annuloplasty. Papillary muscle approximation in patients with ischemic MR improved MV leaflet coaptation because of normalization of the geometric position of papillary muscle/chord heads. Such combination resulted in a lesser number of MR recurrences. Decreased EDV and delayed processes of LV remodeling led to an increase in LV EF and downgrading of NYHA functional class [28–31]. In addition, it was proved that the procedure is safe in immediate and long-term follow-up [32].

Our findings also confirmed the above concept. In the group of patients who had undergone additional repair of subvalvular structures of the mitral valve (papillary muscle approximation), much better echocardiographic parameters of the mitral valve (MV gradient, coaptation line and depth, interpapillary distance) were obtained. Also, the frequency of MR recurrences in the group of patients with papillary muscle approximation was well below that in the group of patients who had undergone isolated annuloplasty.

While analyzing the results obtained and those described in similar studies, we came to the conclusion that additional surgical correction of the subvalvular apparatus combined with mitral annuloplasty is a safe procedure leading to better durability of MV plasty as compared with isolated annuloplasty.

Limitations

The main limitation is a short follow-up and a retrospective nature of the study. We are planning to do further research to achieve long-term outcomes. However, to determine the viability of this procedure, from our viewpoint, large randomized (multi-center) studies are required to reach this goal.

Conclusion

Additional approximation of papillary muscles performed during mitral valve annuloplasty increases the lifetime of mitral valve plasty.

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Conflict of interest

Authors declare no conflict of interest.

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