Risk factors for the return of mitral regurgitation after coronary artery bypass grafting and mitral valve reconstruction in patients with ischemic cardiomyopathy

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Abstract

Background and Aim: We aimed to identify risk factors for recurrent mitral regurgitation in two surgical treatment groups: isolated coronary artery bypass grafting (CABG) and coronary artery bypass grafting combined with mitral valve (MV) repair in patients with moderate ischemic mitral regurgitation (IMR).

Methods: A single-centre, prospective, randomised study, which included 76 patients with ischemic cardiomyopathy (left ventricular ejection fraction less than 35%) and moderate mitral regurgitation. Patients were randomised into two groups: isolated coronary artery bypass grafting and coronary artery bypass grafting with mitral valve repair (MVR). The patients' age was 57.5 ± 8.6 (from 30 to 75) years old. Isolated annuloplasty with a rigid 26–30 mm ring was used to correct mitral insufficiency in the CABG + MVR group.

Results: Isolated coronary artery bypass grafting or coronary artery bypass grafting combined with MVR in patients with ischemic cardiomyopathy (ICM) does not lead to a statistically significant decreasing of mitral regurgitation in the long-term period compared to baseline values. However, in one year after surgery, the degree of mitral regurgitation after combined surgery is lower than the initial values, in contrast to isolated coronary bypass grafting, during the observation period up to 36 months. The degree of mitral regurgitation after isolated CABG corresponds to the initial values. The identification of predictors of the progression of ischemic mitral regurgitation in ICM made it possible to determine the threshold values for the effectiveness of MVR, and the assessment of echocardiographic predictors for annuloplasty before surgery helps to choose the right surgical tactic of patients with ischemic cardiomyopathy and moderate mitral insufficiency.

Conclusions: Coronary revascularisation with surgical of ischemic mitral regurgitation in patients with ischemic cardiomyopathy does not increase the number of complications in the early postoperative period compared to the group of isolated coronary artery bypass grafting ($p = 0.015$). In patients with ischemic cardiomyopathy and moderate mitral regurgitation after isolated coronary artery bypass grafting, the progression of mitral regurgitation (MR of the 3rd degree, initially 0%, after 12 months 31%, after 36 months 71%; $p < 0.001$) was observed even with an initially moderate expansion of the fibrous ring of the mitral valve.

Keywords: Ischemic cardiomyopathy, ischemic mitral regurgitation, mitral insufficiency, coronary artery bypass grafting, mitral annuloplasty.

1 Introduction

Mitral regurgitation (MR) is an unfavourable factor in long-term prognosis in patients with ischemic left ventricular dysfunction (1, 2). It aggravates the course of heart failure, increases the incidence of atrial fibrillation, as well as sudden death (3, 4). The progression of mitral valve insufficiency in ischemic myocardial dysfunction is caused by postinfarction remodelling that increases the volume of the left ventricle (LV) and impaired geometry, and dysfunction of the valve apparatus and papillary muscles (5, 6, 7, 8). As a result of these changes, MR correction with an annuloplastic ring does not eliminate all failure causes (9). Although the pathophysiology of ischemic mitral dysfunction is well studied, there is no consensus on the correction of this pathology, especially in ischemic cardiomyopathy (ICM). Isolated myocardial revascularisation has a better early prognosis due to a lower frequency of perioperative events and a 30-day mortality rate. However, it does not correct MR; and, therefore, it does not stop further cardiac remodelling and does not affect both the functional status of patients and the prognosis of life in the long-term period. On the other hand, additional mitral valve reconstruction is a more traumatic and time-consuming procedure with a higher risk of early complications. In addition, the question of the validity of this intervention in mild and moderate ischemic mitral regurgitation (IMR) remains controversial (10, 11, 12).

The study aims to identify risk factors for recurrent mitral regurgitation in two groups: isolated coronary artery bypass grafting (CABG) and coronary artery bypass grafting combined with surgical correction of moderate mitral regurgitation).

2 Material and methods

A single-centre, prospective, randomised study was conducted, which included 76 patients with ischemic cardiomyopathy (left ventricular ejection fraction (LVEF) less than 35%) and moderate MR. Patients meeting the following criteria were included in the study: age over 18 years, moderate IMR, hemodynamically significant coronary artery disease, LVEF less than 35%. Exclusion criteria: hemodynamically significant structural changes in the heart valves, acute coronary events, severe comorbidities with a life expectancy of fewer than five years. Echocardiographic criteria for moderate ischemic mitral regurgitation are presented in Table 1. The study was approved by the institutional review board of the National Medical Research Center named after academician E.N. Meshalkin. Written informed consent was obtained from eligible patients who agreed to participate in the study.

The G*Power 3.1 application was used to estimate the required sample size. The sample size was calculated according to the superiority design assuming a survival rate of 60% and 30% in CABG patients with MVR and isolated CABG, respectively, and a superiority margin of 0%, based on the results of a study on the survival of patients with moderate MR [13]. In a study by F. Grigioni et al., statistically significant differences in survival were obtained in patients with and without moderate MR: 62 and 29%, respectively. Based on these data, the planned number of patients in both groups was 70, which will be enough to obtain statistically significant differences in long-term survival with the probability of type I and II errors of 0.05 and 0.20, respectively. Considering the possibility of 10% of incomplete observations due to the loss of patients at different stages of follow-up, the total sample size was 77 patients. Patients were randomised into two treatment groups: isolated CABG (control) and CABG with MVR (study). A follow-up check-up was done before surgery, before discharge, one year, three years and five years after surgery. The following examinations were performed: general examination, echocardiography, and 6-minute walk test.

All operations were performed using cardio-pulmonary bypass with cannulation of the ascending aorta and right atrium (isolated CABG group) or separate cannulation of the vena cava (CABG+ MVR group). "Custodiol" (20 ml/kg of patient's body weight) was used to protect the myocardium during aortic occlusion. In 95% of cases, coronary revascularisation was performed using the internal mammary artery to bypass the left anterior descending artery. In 4 (5%) patients no arterial conduits were used due to low quality of conduits. In 6 (7%) cases both mammary and radial arteries were used. Surgical correction of mitral regurgitation was performed with a rigid rings ranging in size from 26 to 30 mm.

2.1 Statistical analysis

The study groups' small size did not allow to test the empirical distributions of continuous data for agreement with the normal distribution law with an error of the second kind less than 20%. Formal testing of normality by the Shapiro-Wilk criterion revealed 22 (48%) normally distributed indicators out of 47 tested. For these reasons, the nonparametric Mann-Whitney U test was used to compare continuous indicators. Descriptive characteristics are presented as mean ± standard deviation for normally distributed data (when described in the text). Median [first quartile; third quartile] for non-normally distributed data when described in the text and for all continuous data in tables; number, the percentage [95% CI] for binary data with the calculation of CI boundaries according to Wilson's formula, for categorical data the number and percentage of patients in each category are given. To check the identity of the distributions of continuous indicators in the groups of CABG and CABG+ MVR, the unpaired Mann-Whitney U-test was used. The shift of distributions was calculated with a 95% confidence interval; within the groups at different time points, the comparison of continuous data was carried out by the paired Mann U-test - Whitney. Comparison of binary and categorical indicators in different groups was carried out by the exact two-sided Fisher test; to compare indicators at different time points within the groups, the McNemar test was used. Comparison of survival between groups was carried out using the logarithmic rank test with the construction of Kaplan - Meier survival curves and the hazard ratio calculation using the Cox proportional hazards model.

Significant predictors of the risk of recurrence of mitral regression were identified by using logistic regression. Individual predictors were determined by constructing univariate models. Before constructing multivariate models, collinear covariates were identified by formally calculating Pearson's correlation coefficients. From the initial multivariate models, including uncorrelated covariants with the achieved level of significance $p < 0.300$ in univariate models, the forward and backward step methods (for double control) using the Akaike information criterion were used to construct optimal multivariate logistic regression models.

The forward and reverse step patterns were the same. Critical values were identified by multivariate logistic regression of the joint predictors of the risk of recurrent MR by exhaustive search.

Statistical hypotheses were tested at a critical level of significance $p = 0.05$, that is, the difference was considered statistically significant at $p < 0.05$. The lower bound of the evidential power is 80%.

Statistical calculations were carried out in the free software RStudio (version 1.1.463, © 2009-2018 RStudio, Inc., USA) in the statistical programming language R: A language and environment for statistical computing (R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R- project.org/).

3 Results

The patients' age was 57.5 ± 8.6 (from 30 to 75) years, men - 90%. The primary demographic data of patients are shown in the Table. 2.

Aortic cross-clamp period in isolated CABG was 48 ± 18 min, and in the CABG+ MVR group - 131 ± 29 min ($p < 0.001$). The average stay of patients in the intensive care unit ranged from 2 to 7 days. All perioperative complications in the two groups were scored at the combined end-point. For this indicator, no difference was found between the groups.
Thus, in the isolated CABG group, complications occurred in 17 patients (44.7%), and in the CABG+ MVR group, in 16 patients (42.1%, $p > 0.999$). Hospital mortality in the CABG group was 2 (5.3%) cases, in the CABG+ MVR group - 4 (10.5%).

Acute heart failure was the leading cause of early mortality in the study. Over a three-year follow-up period, the following complications were noted: acute cerebrovascular accident, sudden cardiac death, progressive heart failure, mitral valve dysfunction (separation of the annuplastic ring) after MV annuloplasty (Table 3). At the same time, there were significantly more complications in the group of isolated CABG - 19 (52.7%) versus 8 (23.5%), $p = 0.015$. In the combined treatment group, an annuloplastic ring detachment, as one of the specific complications, was noted in 4 patients (11.7%), which led to an aggravation of MR ($p = 0.051$). The structure of complications in two groups is shown in the Table. 3.

The analysis of survival for each type of surgical treatment showed a statistically significant difference, so the five-year survival rate after CABG alone was 44 [30; 63]%, and in the group of CABG+ MVR - 73 [60; 89]% (log-rank test, $p = 0.037$) (Fig. 1). For the first two years after surgery, there are no significant differences between the groups (1 and 2 years after surgery, the survival rate is 84 and 78% in the GABG+ MVR group, 84 and 71% in the isolated CABG group). By the third year after surgery, the survival rate in the groups was statistically significantly different. According to the Cox model, the survival analysis showed a 0.5-fold lower risk of death after combined surgery compared to the risk of mortality in the group of isolated coronary artery bypass grafting (RR 0.46 [0.22; 0.97], p = 0.037).

3.1 Dynamics of the clinical and functional status of patients in the long-term period

In the studied groups, the overwhelming number of patients suffered from exertional angina at the levels of II and III functional classes. After a year of observation, a significant decrease in the severity of angina pectoris symptoms was obtained, while in some patients the symptoms were entirely resolved, and in 80% of angina pectoris began to correspond to functional class I. Also, there was an increase in exercise tolerance according to the 6-minute walk test results in two groups. Thus, the average distance increased from 280 to 420 m after 12 months in the isolated CABG group (paired Mann-Whitney U-test, $p = 0.010$) and from 303 to 510 m in the CABG+ MVR group (paired Mann-Whitney U-test, $p < 0.001$).

These indicators correlate with the positive dynamics of the course of heart failure and an improvement in the function of the heart. Left ventricular contractility in the combined treatment group improved from 31.5 [24.75; 34.00] to 33 [28; 38]% in one year after surgery and remained above baseline values up to three years after surgery (paired Mann-Whitney U-test, $p < 0.001$). In the isolated CABG group, an improvement in LV contractility was also noted in the immediate postoperative period, but the contractility significantly decreased during the follow-up period. A year after surgery LVEF changed from 31.5 [27.75; 34.00] to 33 [27.00; 37.25] %, paired U-Mann-Whitney test, $p = 0.020$ and three years after the operation again returned to 30 [24; 32] %, which did not have a statistically significant difference compared to the initial data (paired Mann-Whitney U-test, $p = 0.230$). Thus, both treatment methods significantly improved left ventricular contractility in the first year after surgery, but after three years, LVEF returned to baseline values with the return of the signs of heart failure.

3.2 Dynamics of ischemic mitral regurgitation

The dynamics of MR was assessed depending on the method of treatment (Fig. 2, 3). The criteria for assessing the severity of MR were following: effective regurgitant orifice (ERO), the ratio of the area of the mitral regurgitation stream to the area of the left atrium, vena contracta (the point in a fluid stream where the diameter of the stream is the least, and fluid velocity is at its maximum). Initially, MR in both groups corresponded to the second degree and did not differ between groups.

Analysis of the data showed that CABG alone did not lead to a decrease in the degree of MR after surgery and in the first year of observation, while it is natural that after the MVR, there was a decrease in MR to 0-1 degree, that is, there was a direct dependence on the method of treatment (McNemar test, $p < 0.001$). Thus, in the first year after surgery, MR decreased by at least 1 degree in 100% of patients after CABG+MVR and only in 28% of patients after isolated CABG. 31% of patients from CABG alone MR progress. After three years of follow-up, an increase in MR grade was found in both groups. Thus, in three years after MVR, patients had a positive trend in 47%, the return of MR of the second degree - in 32% of cases and more than 2nd degree - in 21% of cases. While after isolated coronary artery bypass grafting MR remained without dynamics in one year and three years after surgery. Nevertheless, three years after combined surgery, MR was statistically significantly less than in the isolated CABG group (two-sided Fisher's exact test, $p < 0.001$).

To identify MR progression factors in the long-term period, preoperative echocardiographic parameters were studied (Table 4). The data of patients in whom MR progressed in 1 and 3 years after surgery were analysed. A univariate logistic regression was performed and it was found that LV volume indicators (end-diastolic and systolic indices, end-diastolic and systolic volumes) in both groups were predictors of MR return (Table 5).

Multivariate regression revealed that, along with the end-systolic index, significant predictors of MR return were MV geometry parameters (Interpapillary muscle distance in diastole, annulo–papillary muscle distance, leaflet coaptation depth) (Table 6).

It has also been established that the return of MR in systolic myocardial dysfunction is directly related to ischemic remodelling of the cardiac cavities, especially the left ventricle. A special predictor role was played by such indicators as LV volumetric indices, LV contractility and restrictive type of dysfunction, that is, the functional anatomy of the MV in ischemic cardiomyopathy mainly depends on the geometry and function of the basal parts of the LV (basal remodelling).

We also assessed the MR return rates' critical values, which allowed us to develop an algorithm for the surgical treatment of such patients. Thus, it was found that mitral valve reconstruction is advisable in patients with the following LV values: end-systolic index less than 70 ml/ m2, ejection fraction more than 30%, the effective orifice area less than 0.3 cm2, an interpapillary distance less than 45 mm, annulo–papillary muscle distance less than 55 mm, coaptation depth less than 7 mm, non-restrictive type of diastolic dysfunction, pulmonary artery pressure less than 45 mm Hg.

4 Discussion

Mitral valve annuloplasty in addition to myocardial revascularisation has long been an effective treatment for mitral regurgitation (14). However, this statement is not entirely applicable to a cohort of patients with moderate mitral regurgitation and ischemic cardiomyopathy: the results of isolated CABG and CABG combined with MVR in such patients are not satisfactory (14, 15). Thus, mitral insufficiency progresses with isolated revascularisation, and with MVR, there is a risk of MR return (16, 17). The unsatisfactory results of the surgical correction of IMR can be explained by a complex and multifactorial mechanism of its formation, as well as ischemic remodelling of the left ventricle in patients with ICM. At the same time, the expansion of the volume of surgery due to additional intervention on the MV increases the number of perioperative complications and mortality.

According to the results of a meta-analysis (2014), which included only 4 of 119 prospective randomised trials, it was found that the combination of myocardial revascularisation with mitral valve reconstruction reduces the rate of return of MR in the mid-term follow-up, but does not affect the geometry and pumping function of the LV, as well as the course of heart failure. Similar results were demonstrated in an earlier meta-analysis, which proved that mitral valve reconstruction combined with myocardial revascularisation did not significantly affect heart failure, contractility, and early mortality (16). However, there are other studies with opposite results (18, 19). In R. De Simone's study, isolated CABG provided a higher survival rate. Another study (19) also did not reveal the advantages of MV annuloplasty in predicting survival up to 8 years of follow-up; however, a significant decrease in MR progression risk was proved. The contradictory results were explained by the heterogeneity of the included patients, the characteristics of the treatment, and the follow-up duration. Thus, a detailed analysis of subgroups in the study of 2014 showed that the difference in the severity of MR progression increased with an increase in the follow-up period.

5 Conclusion

According to our work results, both isolated CABG and myocardial revascularisation combined with mitral valve annuloplasty in ischemic cardiomyopathy did not contribute to the improvement of MR in the long-term period. At the same time, the degree of MR in 1 year after a combined intervention (CABG+ MVR) was less than preoperative values, in contrast to isolated CABG, and three years after isolated CABG, mitral insufficiency corresponded to preoperative values. Determination of MR return factors in ischemic cardiomyopathy helped to identify the limiting values of the effectiveness of mitral annuloplasty, and the assessment of the initial echocardiographic predictors for annuloplasty made it possible to choose a strategy for surgical treatment of patients with this severe pathology.

Figure legends:

Figure 1. Survival of patients with moderate MR and IC depending on the method of treatment.

Figure 2. Dynamics of MR in the CABG group.

Figure 3. Dynamics of MR in the CABG group combination with MV repair.

References

1. Trichon B. et al. Relation of frequency and severity of mitral regurgitation to survival among patients with left ventricular systolic dysfunction and heart failure. The American Journal of cardiology. 2003; 91(5): 538-543. https://doi.org/10.1016/s0002-9149(02)03301-5.
2. Unger P. et al. Ischemic mitral regurgitation: not only a bystander. Current cardiology reports. 2012; 14(2): 180-189. https://doi.org/10.1007/s11886-011-0241-y.
3. Grigioni F. et al. Atrial fibrillation complicating the course of degenerative mitral regurgitation: determinants and long-term outcome. Journal of the American College of Cardiology. 2002; 40(1): 84-92. http://doi.org/10.1016/s0735-1097(02)01922-8.
4. Grigioni F. et al. Sudden death in mitral regurgitation due to flail leaflet. Journal of the American College of Cardiology. 1999; 34(7): 2078-2085. http://doi.org/10.1016/s0735-1097(99)00474-x.

5. Marchenko A., Cherniavsky A., Volokitina T., Alsov, S., Karaskov A. Left ventricular dimension and shape after postinfarction aneurysm repair. European Journal of Cardio-Thoracic Surgery. 2005; 27(3): 475–480. https://doi.org/10.1016/j.ejcts.2004.12.025.
6. Rogers J., Bolling S. What to do with functional mitral regurgitation: what do we really know and how can we find out? European Journal of Cardio-Thoracic Surgery. 2012; 42(6): 915-917. https://doi.org/10.1093/ejcts/ezs472.
7. Bolling S., Pagani F., Deeb G. et al. Intermediate-term outcome of mitral reconstruction in cardiomyopathy. The Journal of Thoracic and Cardiovascular Surgery. 1998; 115: 381-388. https://doi.org/10.1016/s0022-5223(98)70282-x.
8. Krishnaswamy A., Gillinov A. M., Griffin B. P. Ischemic mitral regurgitation: pathophysiology, diagnosis, and treatment. Coronary artery disease. 2011; 22(5): 359-370. http://doi.org/10.1097/mca.0b013e3283441d3f.
9. Braun J., Klautz R. Functional Mitral Regurgitation: The Surgeons' Perspective. Translational Approach to Heart Failure. 2013; 241-290. https://doi.org/10.1007/978-1-4614-7345-9_10.
10. Castleberry A. W. et al. Surgical revascularisation is associated with maximal survival in patients with ischemic mitral regurgitation: a 20-year experience. Circulation. 2014; 129(24): 2547–2556. http://doi.org/10.1161/circulationaha.113.005223.
11. Cohn J. N., Tognoni G. A randomised trial of the angiotensin-receptor blocker valsartan in chronic heart failure. New England Journal of Medicine. 2001; 345 (23) 1667-1675. http://doi.org/10.1056/nejmoa010713.
12. Cherniavsky A.M., Yefremova O.S., Ruzmatov T.M., Efendiyev V.U. Predictors of remote mortality of CHD patients with severe left ventricular dysfunction. Patologiya krovoobrashcheniya i kardiokhirurgiya = Circulation Pathology and Cardiac Surgery. 2015;19(2):49-54. (In Russ.). http://dx.doi.org/10.21688/1681-3472-2015-2-49-54.

13. Grigioni F. et al. Ischemic mitral regurgitation long-term outcome and prognostic implications with quantitative Doppler assessment //Circulation. – 2001. – T. 103. – №. 13. – C. 1759-1764

14. Kron I. L. et al. Predicting recurrent mitral regurgitation after mitral valve repair for severe ischemic mitral regurgitation. The Journal of thoracic and cardiovascular surgery. 2015; 149 (3): 752-761. e1. http://doi.org/10.1016/j.jtcvs.2014.10.120.

15. Jeong D. S. et al. Off pump coronary artery bypass versus mitral annuloplasty in moderate ischemic mitral regurgitation. Annals of Thoracic and Cardiovascular Surgery. 2012; 18(4): 322- 330. http://doi.org/10.5761/atcs.oa.11.01845.

16. McMurray J. J. V. et al. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012. European Journal of heart failure. 2012; 14(8): 803-869. http://doi.org/10.1093/eurjhf/hft016.

17. Fattouch K. et al. Impact of moderate ischemic mitral regurgitation after isolated coronary artery bypass grafting. The Annals of thoracic surgery. 2010; 90(4): 1187-1194. http://doi.org/10.1016/j.athoracsur.2010.03.103.

18. Di Donato M., Sabatier M., Dor V., et al. Impact of no-to moderate mitral regurgitation on late results after isolated coronary artery bypass grafting in patients with ischemic cardiomyopathy. The Annals of thoracic surgery. 2006; 81(6): 2128-2134. http://doi.org/10.1016/j.athoracsur.2006.01.061.

19. De Simone R. et al. A clinical study of annular geometry and dynamics in patients with ischemic mitral regurgitation: new insights into asymmetrical ring annuloplasty. European Journal of cardio-thoracic surgery. 2006; 29(3): 355-361. http://doi.org/10.1016/j.ejcts.2005.12.034.

TABLE 1. Echocardiographic parameters of moderate IMR

Indicator	CABG Med [IQR]	CABG+MVR Med [IQR]	Odds Med [95% CI]	Mann - Whitney U test, p
ERO, cm^2	0.3 [0.25; 0.32]	0.3 [0.27; 0.35]	0 [-0.02; 0.03]	0.790
S_{MR}/S_{LA}	30 [24.25; 35.75]	35 [25.5; 37.0]	2 [0; 5]	0.110
TA, cm^2	1.75 [1.52; 1.87]	1.8 [1.5; 2.0]	0 [-0.1; 0.2]	0.710
CD, mm	7 [6; 8]	8 [7; 9]	1 [0; 2]	0.088
CL, mm	2.5 [2; 3]	3 [2; 3]	0 [0; 1]	0.635
IPMD, mm	46.5 [38; 50]	47 [37.25; 52.00]	0 [-3; 4]	0.819
APMD, mm	55 [50.25; 56.75]	52 [46; 57]	-2 [-5; 1]	0.196
MVD, mm	37 [35.25; 39.75]	37 [35; 39]	-1 [-2; 1]	0.389

Note. ERO- effective regurgitant orifice, Med- median, IQR- interquartile range, CI - confidence interval, S_{MR}/S_{LA}- the ratio of the area of the mitral regurgitation stream to the area of the left atrium, TA- mitral valve tenting area, CD- coaptation depth, CL- coaptation length, IPMD- Interpapillary muscle distance in diastole, APMD- annulo–papillary muscle distance, MVD - mitral valve diameter.

TABLE 2: Preoperative characteristics of patients included in the study

Indicator		**CABG** **Med [IQR]**	**CABG+MVR** **Med [IQR]**	**Odds** **Med [95% CI]**	**Mann - Whitney U test, p**
Male		34 (89.4%)	30 (78.9%)	0.4 [0,1; 1.9]	0.346
Female		4 (10.6%)	8 (21.1%)	2.2 [0.5;11.2]	0.346
Age		56 [53.0; 63.5]	58 [51.00; 64.75]	0 [-4; 4]	0.913
Chronic renal failure		2 [1; 17]	7 [9; 33]	4[0.7; 42.2]	0.153
Myocardial infarction		36 [83; 99]	36 [83; 99]	1 [0.1; 14.5]	>0.999
Hypertension		28 [58; 85]	29 [61; 87]	1.1 [0.4; 3.7]	>0.999
Diabetes mellitus		8 [11; 36]	7 [9; 33]	0.8 [0.2; 3.1]	>0.999
Atrial fibrillation		6 [7; 30]	10 [15; 42]	1.9 [0.5; 7.2]	0.399
Stroke		2 [1; 17]	3 [3; 21]	1.5 [0.2;19.4]	>0.999
	I	0	0	–	>0.999

NYHA, n(%)					
	II	5 (13.2%)	4 (10.5%)	1.3 [0.3; 7.1]	>0.999
	III	22 (57.9%)	25 (65.8%)	0.7 [0.3; 2.0]	0.637
	IV	11 (28.9%)	9 (23.7%)	0.7 [0.3; 2.0]	0.795
Angina pectoris grade, CCS, n(%)	Without angina	8 (21%)	8 (21%)	1.0 [0.3; 3.5]	>0.999
	I	4 (10.5%)	5 (13%)	0.8 [0.1; 4.0]	>0.999
	II	12 (31.5%)	12 (31.5%)	1.0 [0.3; 2.9]	>0.999
	III	11 (29%)	11 (29%)	1.0 [0.3; 3.0]	>0.999
	IV	3 (7.9%)	2 (5.2%)	1.5 [0.2;19.4]	>0.999

Note: Comparison of age was performed by unpaired Mann-Whitney U-test with the calculation of the shift of distributions [95% CI of shift], all other indicators were compared with Fisher's exact two-sided test with the calculation of the odds ratio [95% CI OR]; Med- median, IQR- interquartile range, CI - confidence interval, NYHA - New York Heart Association, CCS- Canadian Cardiovascular Society classification.

TABLE 3. Complications in the long-term postoperative period.

Complication	**CABG n=36 (50%)**	**CABG + MV repair n=36 (50%)**	**CABG/CABG + MV repair Risk ratio**	**P-value**
Stroke	4 (11.1%)	0	8.5	0.115
Sudden cardiac death	4 (11.1%)	1 (2.9%)	3.78	0.358
Heart failure	11 (44%)	5 (14.7%)	2.08	0.157
The detachment of the	0	4 (11.7%)	-	0.051

annuloplastic ring				
Combined point	19 (52.7%)	8 (23.5%)	2.24	0.015

TABLE 4. Preoperative values of the risk covariants of mitral regurgitation progression

Covariants	CABG, n = 38	CABG + MV repair, n= 38	Difference	p-value	CABG/CABG + MV repair Risk ratio, n = 76
EDI	106.9 [97.4; 119.6]	99.8 [88.2; 127.5]	-4.4 [-15.2; 7.3]	0.411	103.8 [92.0; 123.7]
ESI	74.4 [67.3; 85.6]	71.1 [58.4; 92.7]	-3.1 [-11.7; 6.1]	0.466	73.9 [65.2; 87.0]
EDV, ml	211.4 [192.3; 234.5]	199.5 [165; 250]	-9 [-33.5; 16]	0.451	208.2 [179.8; 241]
ECV, ml	148 [133.3; 162]	147 [111; 175.3]	-5 [-24; 14]	0.557	148 [123.5; 171]
EF, %	31 [27; 33.75]	30.5 [23.25; 34]	0 [-3; 2]	0.707	31 [24; 34]

S_{MR}/S_{LA}	30 [24.25; 35.75]	35 [25.5; 37]	2 [0; 5]	0.110	32 [25; 36.25]
ERO, cm^2	0.31 [0.27; 0.34]	0.3 [0.27; 0.35]	0 [-0.02; 0.03]	0.790	0.305 [0.27; 0.34]
MVD, mm	37 [35.25; 39.75]	37 [35; 39]	-1 [-2; 1]	0.389	37 [35; 39]
TA, cm^2	1.75 [1.52; 1.87]	1.8 [1.5; 2]	0 [-0.1; 0.2]	0.710	1.8 [1.5; 2]
IPMD, mm	46.5 [38; 50]	47 [37.25; 52]	0 [-3; 4]	0.819	46.5 [38; 51.25]
APMD, mm	55 [50.25; 56.75]	52 [46; 57]	-2 [-5; 1]	0.196	54.5 [48.75; 57]
CD, mm	7 [6; 8]	8 [7; 9]	1 [0; 2]	0.088	8 [6; 9]
Dysfunction type, n(%)	1 - 15 (40%) 2 - 23 (60%)	1 - 15 (40%) 2 - 23 (60%)		>0.999	1 - 30 (40%) 2 - 46 (60%)
RA, cm^2	5.85 [5.24; 6.2]	5.85 [4.78; 6.3]	-0.1 [-0.5; 0.3]	0.603	5.85 [4.97; 6.3]
CL, mm	2.5 [2; 3]	3 [2; 3]	0 [0; 1]	0.635	3 [2; 3]
Diastolic LV dysfunction, initial	1 - 19 (50%) 2 - 11 (29%)	1 - 10 (26%) 2 - 21 (55%)		0.054	1 - 29 (38%) 2 - 32 (42%)

	3 - 8 (21%)	3 - 7 (19%)			3 - 15 (20%)
LA, cm^2	5.2 [4.85; 5.68]	5.57 [5.3; 5.88]	0.3 [0; 0.58]	0.033*	5.4 [5.08; 5.77]
P_{PA}	39.5 [35; 49.75]	42.5 [38; 55.75]	3 [-2; 7]	0.255	42 [35.75; 53.25]
TR	0 - 0 (0%) 1 - 19 (51%) 2 - 16 (43%) 3 - 2 (6%)	0 - 1 (3%) 1 - 20 (54%) 2 - 16 (43%) 3 - 0 (0%)		0.613	0 - 1 (1% 1 - 39 (3%) 2 - 32 (43%) 3 - 2 (3%)

Note. EDI - end-diastolic index, ESI - end-systolic index, EDV - end-diastolic volume, ESV - end-systolic volume, EF - ejection fraction, S_{MR}/S_{LA}- the ratio of the area of the mitral regurgitation stream to the area of the left atrium, ERO- effective regurgitant orifice, MVD - mitral valve diameter, TA- mitral valve tenting area, CD- coaptation depth, CL- coaptation length, IPMD- Interpapillary muscle distance in diastole, APMD- annulo–papillary muscle distance, LV - left ventricle, LA - pulmonary artery, P_{PA}- pulmonary artery pressure, TR- tricuspid regurgitation. Comparison of the type of dysfunction, baseline LV diastolic dysfunction and tricuspid regurgitation was carried out by the exact two-sided Fisher test, the comparison of the remaining covariants was performed by the unpaired Mann-Whitney U test with the calculation of the shift in distributions and a shift in the 95% confidence interval.

TABLE 5. Model of univariate logistic regression of the risk of progression of MR in the long-term period

Predictors	**Odds ratio MR/no MR**	**95% odds ratio CI**	**p-value**
EDI	1.042	[1.003; 1.097]	0.06
ESI	10.49	[1.006; 1.109]	**0.04**
EDV	1.021	[1.005; 1.047]	**0.03**
ESV	1.025	[1.005; 1.055]	**0.03**
EF	0.885	[0.746; 1.03]	0.12
S_{MR}/S_{LA}	1.052	[0.901; 1.253]	0.52
ERO	0.187	[0; 33929.04])	0.84
MVD	1.094	[0.837; 1.465]	0.51
TA	0.441	[0.038; 4.226]	0.48
IPMD	1.033	[0.943; 1.145]	0.48
APMD	0.965	[0.862; 1.074]	0.51
CD	1.009	[0.63; 1.629]	0.96
Disfunction type	1.285	[0.241; 7.208]	0.76
RA	0.752	[0.267; 2.009]	0.57

CL	0.941	[0.422; 2.064]	0.87
Diastolic LV dysfunction, initial	1.308	[0.383; 4.805]	0.66
LA	1.864	[0.45; 9.351]	0.40
P_{LA}	0.991	[0.918; 1.066]	0.80
TR	0.484	[0.085; 2.249]	0.36

Note. EDI - end-diastolic index, ESI - end-systolic index, EDV - end-diastolic volume, ESV - end-systolic volume, EF - ejection fraction, S_{MR}/S_{LA}- the ratio of the area of the mitral regurgitation stream to the area of the left atrium, ERO- effective regurgitant orifice, MVD - mitral valve diameter, TA- mitral valve tenting area, CD- coaptation depth, CL- coaptation length, IPMD- Interpapillary muscle distance in diastole, APMD- annulo–papillary muscle distance, LV - left ventricle, LA - pulmonary artery, P_{PA}- pulmonary artery pressure, TR- tricuspid regurgitation.

TABLE 6. Model of univariate logistic regression of the risk of progression of mitral regurgitation in the long term

Predictors	**Odds ratio MR/no MR**	**95% odds ratio CI**	**p-value**
ESI	1.043	[0.929; 1.206]	**0.04**
EF	0.845	[0.529; 1.173]	0.06
ERO	[0; +∞]	[0; +∞]	0.16
IPMD	1.223	[0.905; 1.822]	**0.05**
APMD	0.680	[0.293; 1.17]	0.07
CD	0.891	[0.226; 5.182]	**0.05**
Diastolic LV dysfunction	1.166	[0.152; 8.664]	**0.04**
P_{LA}	0.990	[0.876; 1.14]	0.06

TR	4.784	[0.424; 215.478]	0.17

Note. ESI - end-systolic index, EF - ejection fraction, ERO- effective regurgitant orifice, CD- coaptation depth, IPMD- Interpapillary muscle distance in diastole, APMD- annulo–papillary muscle distance, LV - left ventricle, P_{PA}- pulmonary artery pressure, TR- tricuspid regurgitation.