ENHANCED REVERSE CARDIAC REMODELING AFTER PULMONARY ARTERY DENERVATION COMBINED WITH MITRAL AND MAZE SURGERY

N.A. Trofimov, A.V. Nikolskiy, A.L. Rodionov, D.V. Egorov, T.V. Surkova*

Chuvash State University, 15 Moskovskiy Prospekt, Cheboksary, 428015, Russia

* Corresponding author: nikolai.trofimov@mail.ru

Abstract. Objectives: the study evaluates the effectiveness of reverse cardiac remodeling in patients after surgical treatment of severe pulmonary hypertension (PH) in patients with mitral valve disease and atrial fibrillation (AF). Methods: the analysis of the surgical treatment of 202 patients with mitral valve disease complicated by PH (more than 40 mmHg) and AF was performed. The surgical intervention consisted in surgical correction of mitral dysfunction (valve replacement or repair) – the group 1 of patients (n = 62). Patients of the second group (n = 89) additionally underwent the Maze IV procedure for concomitant AF using the AtriCure bipolar radiofrequency ablator. Patients of the group 3 (n = 51) underwent a complex surgical intervention consisting of mitral valve surgery, AF correction using Maze IV, circular radiofrequency denervation of the trunk and orifices of the pulmonary arteries (PA) (Pulmonary Artery Denervation - PADN). Results: PADN can significantly reduce the level of LH in the postoperative period ($p\chi^2 = 0.018$ compared with other groups) and promotes reverse cardiac remodeling by reducing its cavities. Complex surgical correction of patients with mitral valve disease, AF and severe PH can significantly reduce the severity of heart failure ($p\chi^2 = 0.023$ compared to the group without PADN). Conclusion: the PADN circular procedure is effective and safe. Further analysis of the effectiveness of PADN with a grouping of a larger number of patients, analysis of long-term results, and determination of the feasibility of this technique in patients with non-valvular forms of PH is needed.

Keywords: secondary pulmonary hypertension, pulmonary arteries denervation, mitral valve disease, atrial fibrillation.

List of Abbreviations

AF – atrial fibrillation

LADs – left atrium anterior-posterior diameter in systole

LVEDV – left ventricular end-diastolic volume

LVEF – left ventricular ejection fraction

LVESV – left ventricular end-systolic volume

LVIDd – left ventricular internal diameter in diastole

LVIDs – left ventricular internal diameter in systole

mPAP - mean pulmonary artery pressure

PA – pulmonary arteries

PADN – pulmonary arteries denervation

PASP – pulmonary artery systolic pressure

PH – pulmonary hypertension

RADs – right atrium anterior-posterior diameter in systole

RVD – right ventricular basal diameter

TVI – tricuspid valve insufficiency

Introduction

In patients with heart valve pathology, increased pressure in the pulmonary circulation reduces the effectiveness of surgical intervention, worsens postoperative reverse cardiac remodeling and also increases the risk of recurrence of AF after radiofrequency ablation using the Maze IV method (Babokin & Trofimov, 2020).

The possibility of correcting PH was discussed by S. Briongos Figuero et al., who demonstrated that a high preoperative PH was closely correlated with the persistence of PH even after surgical treatment of mitral valve disease (odds ratio 1.761; p = 0.03) (Briongos Figuero *et al.*, 2016). The location of the sympathetic nerve plexuses in the adventitia of the trunk and orifices of the PA, which are responsible for spasm of the pulmonary arterioles and an increase in PH, was first reported in the works of J. Osorio in 1962 (Osorio & Russek, 1962). These data were subsequently confirmed by B.G. Baylenet et al. (Baylen *et al.*, 1980) and C.E. Juratschet et al. (Juratsch *et al.*, 1980).

Currently, conservative treatment of high PH does not allow achieving a stable reduction in pressure in the pulmonary circulation and is associated with the use of expensive drugs (Guazzi *et al*., 2012).

The first surgical interventions for high PH were proposed by S.L. Chen in 2013 in the form of endovascular catheter ablation of the trunk and orifices of the PA, which, according to the authors, significantly reduced the pressure in the PA (Chen *et al*., 2013). In recent years, several works have been presented on the surgical correction of PH simultaneously with the correction of mitral valve disease under conditions of cardiopulmonary bypass. A technique for radiofrequency ablation of the anterior wall of the trunk and orifices of the pulmonary arteries with a monopolar electrode was proposed. Moreover, currently used is the method of circular radiofrequency denervation of the PA using a bipolar radiofrequency clamp is currently used (Trofimov *et al*., 2009; Trofimov *et al.*, 2019).

Despite the existing methods of PH correction, the problem of surgical treatment of severe secondary PH is the most relevant, since there is no generally accepted algorithm for the treatment of this pathology, further study of the problem with the search for the optimal surgical technique for this category of patients is necessary.

Materials and Methods

The study analyzed the surgical treatment of 202 patients with mitral valve disease complicated by severe PH (mPAP over 40 mmHg) and AF. Patients underwent surgical correction of mitral disease – valve repair or replacement - the first group of patients (n = 62). Patients of the second group (n = 89) also underwent correction of mitral valve disease, as well as the Maze IV procedure due to concomitant AF using the AtriCure bipolar radiofrequency ablator. Patients of the third group (n = 51) underwent a complex surgical intervention, consisting of intervention on the mitral valve, surgical correction of AF using the Maze IV procedure, and circular PADN. Inclusion criteria were mitral valve defects complicated by AF and severe secondary PH. The exclusion criteria were a history of pulmonary embolism, hemodynamically significant coronary artery disease. The study was approved by the local ethics committee, registration number 10/D-2019 dated May 26, 2019. Without fail, all the studied patients before the operation were informed about the forthcoming additional procedure for PADN, which was planned to be performed with the main stage of surgical correction. Informed voluntary consent was signed, in accordance with Good Clinical Practice and the Declaration of Helsinki.

The patients of all study groups were comparable in terms of the main clinical and instrumental indicators (Table 1). The presented data characterize patients of the 3rd group as more severe in terms of age, EuroSCORE, left ventricular contractility, left ventricular and right heart dilatation, and PH severity.

The PADN procedure was performed circularly using AtriCure's Isolator Synergy Bipolar RF Clamps. After mobilization of the pulmonary trunk and orifices of the PA under conditions of a beating heart with simultaneous use of cardiopulmonary bypass, 2 circular ablation lines were applied to the distal pulmonary trunk, each line consisting of 3 applications (Fig. 1A). Then, the orifice of the right PA was isolated and similar circular ablation lines were applied (Fig. 1B). In some cases, the right PA was isolated by subaortic access, to the right of the aorta, in the transverse sinus of the heart. Similarly, circular denervation of the orifice of the left PA was performed (Fig. 1C). The procedure resulted in 6 ablation lines, 2 at the level of the distal pulmonary trunk and 2 at the level of the orifices of PA (Fig. 1D).

The mean total PADN procedure time was 5.5 minutes. After radiofrequency denervation of the PA, antegrade custodiol cardioplegia was performed into the aortic root. After cardiac arrest, the main stage of the operation was performed – correction of valvular disease and the Maze IV procedure. The mean total aortic cross-clamping time was 85.2 minutes, the time of cardiopulmonary bypass was 114.1 minutes. Patients were in the intensive care unit for an average of 2.4 days. Postoperative management of patients in the denervation group did not dif-

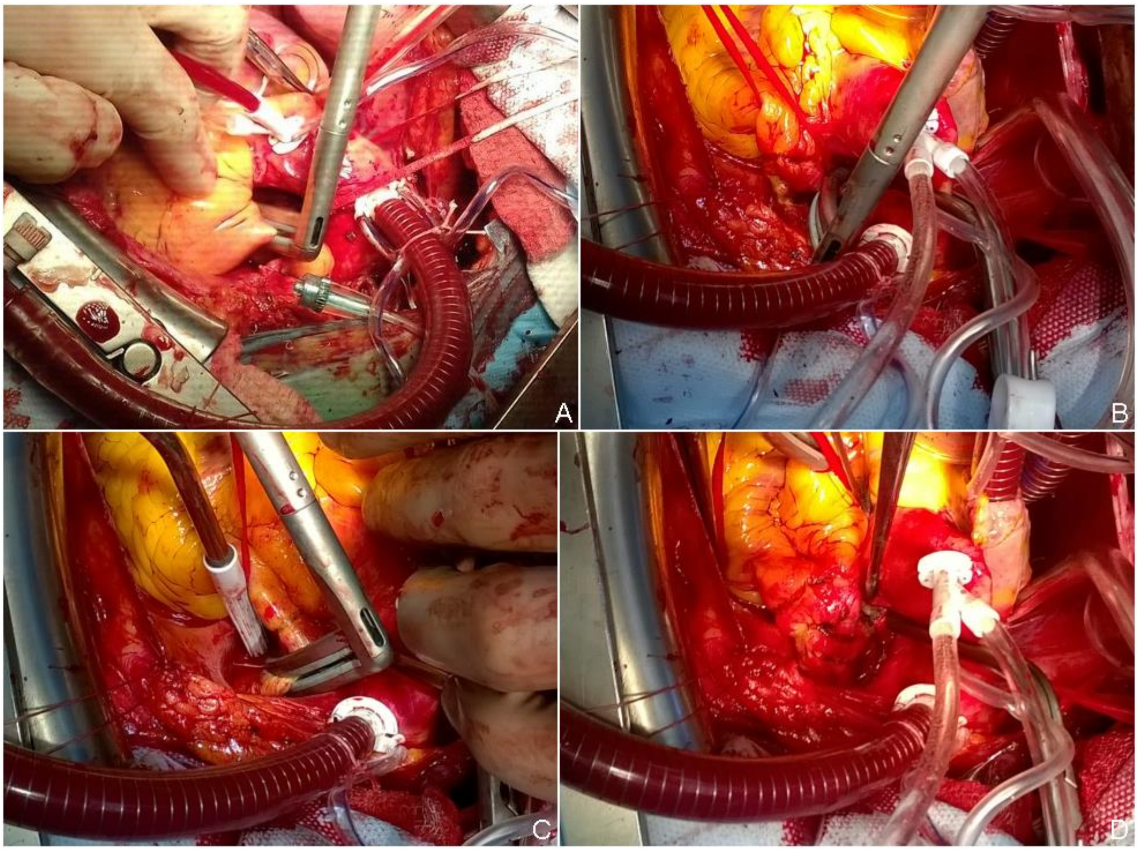

Fig. 1. Stages of circular PADN: A – circular ablation of the pulmonary trunk; B – ablation of the orifice of the right pulmonary artery; C – ablation of the orifice of the left pulmonary artery; D – the final view of the circular PADN procedure

fer from the management of patients in other groups. All patients were followed up with periodic visits under ECHO control 3, 6, 12, 24 months after surgery.

Statistical processing of the results was carried out in the program "SPSS Statistics 26". Quantitative data were presented as mean and standard deviation (M ± σ), with rank values or skewed distribution as median and upper and lower quartiles (Me; {Q1-Q3}).

The statistical significance of differences for quantitative data with a normal distribution was assessed using the Student's t-test, and for skewed distribution and for rank data - using the Mann-Whitney U-test. The normality of distribution was tested using the Shapiro-Wilk test. For qualitative data (relative values), differences were assessed using Pearson's chi-square test (χ^2). If the number of observations in at least one of the fields in Table 2 was less than 5, the calculation was made using Fisher's exact test. If it was necessary to simultaneously compare the three groups, the Kruskal-Wallis test (for quantitative and rank data) and the chi-square test (for qualitative data) were used. The error probability (p) was considered acceptable at $p < 0.05$. With the successive repeated application of Student's statistical tests, chi-square and Mann-Whitney (alternate comparison of groups among themselves), the probability of detecting differences where there are none increased N times. Therefore, in a triple sequential comparison of groups, the Bonferroni correction was used, the acceptable level of significance (p) was calculated as $p = 0.05/n$, where $n = 3$, i.e., 0.0167. The statistical significance of dynamic differences was calculated for quantitative data using the Wilcoxon signed-rank test, for qualitative data using the McNemar test with Yates correction. Statistical analysis was based on the recommendations of Stanton A. Glantz.

Table 1

Clinical and instrumental characteristics of the studied patients (n = 202)

	Group 1	Group 2	Group 3	*p* Value		
	(n = 62)	(n = 89)	(n = 51)	1–2	1–3	2–3
Gender (male/female)	19/43	28/61	23/28	0.916	0.116	0.108
Age at operation, years	56.3 ± 8.0	55.8 ± 8.3	59.4 ± 5.2	0.740	0.017#a	0.005#
Cause of mitral valve disease, %						
Rheumatic fever	82	85	76	0.604	0.447	0.184
Infective endocarditis	8	9	20	0.842	0.073	0.072
Degenerative	10	6	4	0.345	0.235	0.657
Type of AF						
Long-term persistent	77	84	86	0.167	0.321	0.749
Persistent	8	2	8	0.094	0.965	0.116
Paroxysmal	15	13	6	0.857	0.138	0.162
Arrhythmia history, years	2.7 ± 2.2	2.7 ± 1.7	2.6 ± 1.4	0.841	0.887	0.688
Atrial flutter, %	10	20	14	0.081	0.501	0.385
Carotid stenosis > 50%, %	27	17	18	0.118	0.219	0.904
Past medical history of a stroke, %	10	8	8	0.867	0.320	1
EuroSCORE	5 (3-6)	4 (3-6)	5 (4-8)	0.817	0.004#	0.004#
Cardiopulmonary bypass time, min	110 (90-136)	136 (118-151)	111 (87-130)	0.006#	0.511	< 0.001#
Aortic cross-clamp time, min	84.5 (70-102)	107 (92-128)	79 (67-102)	< 0.001#	0.359	< 0.001#
TVI 2-4 degree, %	54.8	76.4	64.7	0.016#	0.533	0.095
NYHA III-IV class, %	27.4	28.1	43.1	0.953	0.082	0.058
LVIDd, cm	5.5 (5.2-6.3)	5.5 (5.2-5.7)	5.6 (5.4-6.4)	0.245	0.349	0.014#
LVIDs, cm	4.2 (3.7-4.8)	3.8 (3.6-4.1)	4 (3.8-4.8)	0.002#	0.925	< 0.001#
LVEDV, cm	147.4 (129.5-201.2)	143.2 (130.4-160)	153.7 (135.3-208.5)	0.176	0.465	0.016#
LVESV, cm	76.4 (58.1-107.5)	62 (54.4-71.2)	70 (62.0-107.5)	0.001#	0.902	< 0.001#
LVEF, %	51 (43.9-57.9)	56.3 (53.1-58)	52.2 (49.1-55.1)	< 0.001#	0.080	< 0.001#
RVD, cm	3.4 (3.2-3.6)	3.4 (3.2-3.7)	3.6 (3.4-4)	0.182	< 0.001#	0.003#
LADs, cm	5.1 (4.8-5.7)	5.4 (5.2-5.6)	5.5 (5.3-5.7)	0.034	0.002#	0.600
RADs, cm	5.2 (5-5.7)	5.6 (5.2-5.9)	5.8 (5.6-6)	0.004#	< 0.001#	0.095
PASP, mmHg	46 (43-49)	46 (44-50)	48 (45-60)	0.440	0.002#	0.018

[a] Hereinafter, for most cases (for the age of patients and AF, Student t-test was used), intergroup differences were calculated by the Mann–Whitney U-test due to skewed distribution (in this case, the data are presented as “Me (Q1-Q3)”), for qualitative values used the Pearson's chi-squared test or the Fisher's exact test. The # sign indicates the required level of statistical significance, taking into account the Bonferroni correction.

Results

Lethal outcomes among patients occurred one in each group and were due to progressive acute heart failure on the first day after surgery. There were no postoperative complications associated with the PADN procedure. According to transthoracic echocardiography, all patients showed improvement in the postoperative period (Table 2). A significant decrease in the frequency of AF was not observed only in the 1st group.

Since the main criterion for evaluating the effectiveness of treatment is the achievement of target indicators, the final results in the study groups are analyzed as a proportion of the indicators achieved. For echocardiographic parameters, the range of normal values was used (Table 3). The table shows that with comparable initial parameters, the achievement of target values in the 3rd group is significantly better, including in comparison with the 2nd group, even taking into account the Bonferoni correction. Positive dynamics according to the McNemar criterion was noted for almost all parameters in the 2nd and 3rd groups. In the 1st group, it was not possible to achieve a statistically significant improvement in the values of the LA and RA sizes, normalization of mPAP, restoration of sinus rhythm.

The presented echocardiographic data demonstrate significant positive changes in the group of complex surgical treatment for reverse cardiac remodeling, decrease in mPAP, increase in the left ventricular ejection fraction, restoration and maintenance of sinus rhythm, compared with groups 1 and 2.

Circular denervation of the sympathetic ganglia in the trunk and orifices of the PA promotes relaxation of the smooth muscle fibers of the vascular wall, which leads to dilatation of the arteries and arterioles, an increase in the capacity of the vascular bed in the pulmonary circulation, and reduces PH in the postoperative period.

During the work, the dynamics of mPAP was analyzed according to the data of transthoracic echocardiography (Fig. 2). The PH parameters in the 3rd group, initially significantly worse, already 3 months after the operation were comparable with those of the 1st and 2nd groups, and subsequently the best parameters among the studied groups. Normalization of PH contributed to a decrease in pressure in the right heart, primarily in the right ventricle, which had a beneficial effect on the reverse remodeling of the right ventricular cavity in the postoperative period (Fig. 3). Also, a significant existing dilatation of the right ventricle after 6 months was comparable in average values with the 1st and 2nd groups, and by 24 months it occupied a leading position among all the studied groups. Concomitant tricuspid valve insufficiency, which was observed in almost all patients and was eliminated during the operation by repair, also had a positive trend in the postoperative period (Fig. 4). The positive effect of surgical correction also affected the reduction of heart failure according to the 6-minute walk test (Fig. 5).

The results presented in the diagram demonstrate a significant advantage of the complex surgical treatment applied in the 3rd group already 3 months after the operation, compared with the 1st and 2nd groups. Elimination of tricuspid insufficiency against the background of a decrease in pressure in the right cavities of the heart contributed to a decrease in the size of the right atrium (Fig. 6A). The presented diagram shows the best dynamics of the reverse cardiac remodeling in the group of complex surgical treatment (group 3) - a more pronounced dilatation of the right atrium before surgery was comparable with the average values of groups 1 and 2, and after 12 months showed the best results among groups under study. The complex surgical approach in group 3 made it possible to increase the efficiency of surgical treatment of AF, which significantly improved the results of restoration and maintenance of sinus rhythm in the postoperative period compared with patients in groups 1 and 2 (Table 2). The restored sinus rhythm contributed to better reverse remodeling of the left atrial cavity (Fig. 6B). The presented data demonstrate a significant reduction in heart failure in group 3 12 months after surgery compared with patients in groups 1 and 2, which is due to positive changes in hemodynamic and structural parameters of the myocardium.

Table 2

Changing of echocardiographic parameters of the studied groups

		Group 1	Group 2	Group 3	*p* Value		
		(n = 62)	(n = 89)	(n = 51)	1-2	1-3	2-3
TVI 2-4 degree, %	original	54.8	76.4	64.7	0.016#[a]	0.533	0.095
	24 months after	32.80*[b]	20.5*	0*	0.044	< 0.001#	< 0.001#
NYHA III-IV class, %	original	100	98.9	100	0.953	0.082	0.058
	24 months after	67.2	36.4*	18.0*	< 0.001#	< 0.001#	0.023
LVIDd, cm	original	5.5 (5.2-6.3)	5.5 (5.2-5.7)	5.6 (5.4-6.4)	0.245	0.349	0.014#
	24 months after	5.3 (5-6)*	4.8(4.6-5.1)*	4.6 (4.5-5.3)*	< 0.001#	< 0.001#	0.896
LVIDs, cm	original	4.2 (3.7-4.8)	3.8 (3.6-4.1)	4 (3.8-4.8)	0.002#	0.925	< 0.001#
	24 months after	3.9 (3.4-4.3)*	3.3 (3.1-3.7)*	3.2 (3-3.6)*	< 0.001#	< 0.001#	0.625
LVEDV, cm	original	147.4 (129.5-201.2)	143.2 (130.4-160.0)	153.7 (135.3-208.5)	0.176	0.465	0.016#
	24 months after	135.3 (118.2-180)*	105.9 (97.3-123.8)*	97.3 (93.8-135.3)*	< 0.001#	< 0.001#	0.858
LVESV, cm	original	76.4 (58.1-107.5)	62.0 (54.4-71.2)	70 (61.9-107.5)	0.001#	0.902	< 0.001#
	24 months after	65.9 (47.4-83.1)*	44.1 (36.5-57.7)*	42.6 (35-54.43)*	< 0.001#	< 0.001#	0.691
LFEV, %	original	51.0 (43.9-57.9)	56.3 (53.1-58.0)	52.2 (49.1-55.1)	< 0.001#	0.08	< 0.001#
	24 months after	53.4 (47.6-57.0)*	57.9 (54.4-63.3)*	58.2 (56.3-60.1)*	< 0.001#	< 0.001#	0.857
RVD, cm	original	3.4 (3.2-3.6)	3.4 (3.2-3.7)	3.6 (3.4-4)	0.182	< 0.001#	0.003#
	24 months after	3.2 (3-3.4)*	3.0 (2.9-3.1)*	2.9 (2.8-3.2)*	< 0.001	< 0.001	0.156
LADs, cm	original	5.1 (4.8-5.7)	5.4 (5.2-5.6)	5.5 (5.3-5.7)	0.034	0.002#	0.600
	24 months after	4.8 (4.5-5.3)*	4.3 (4-4.6)*	4.1 (3.8-4.3)*	< 0.001#	< 0.001#	0.010#
RADs, cm	original	5.2 (5-5.7)	5.6 (5.2-5.9)	5.8 (5.6-6)	0.004#	< 0.001#	0.095
	24 months after	5.1 (5-5.5)*	5.0 (4.4-5.3)*	4.5 (4.4-5)*	< 0.001#	< 0.001#	0.073
PASP, mmHg	original	46 (43-49)	46 (44-50)	48 (45-60)	0.44	0.002#	0.018
	24 months after	32 (30-34)*	26 (23.5-29.4)*	23 (21-28)*	< 0.001#	0.583	0.519
AF, %	original	100	100	100	1	1	1
	24 months after	95	34*	16*	< 0.001#	< 0.001#	0.022

[a] Intergroup differences were calculated using the Mann-Whitney U-test due to skewed distribution (in this case, the data are presented as “Me (Q1-Q3)”), for qualitative values Pearson's chi-square test or Fisher's exact test were used. The # sign indicates the required level of statistical significance, taking into account the Bonferroni correction.

[b] The statistical significance of dynamic differences was indicated by the * sign in the data line after 24 months, for quantitative data it was evaluated by the Wilcoxon signed-rank test, for analysis of repeated measurements of qualitative characteristics – by the McNemar test with Yates correction (changes in the percentage of TVI 0-1 degree, the NYHA II-IV share, AF percentage).

Table 3

The share of target indicators 24 months after surgery in the study groups

		Group 1	Group 2	Group 3	*p* Value		
		(n = 62)	(n = 89)	(n = 51)	1-2	1-3	2-3
TVI 0-1 degree, %	original	45.2	23.6	35.3	0.005#a	0.288	0.137
	24 months after	67.2*b	79.5*	100*	0.089	< 0.001#	< 0.001#
TVI 0 degree, %	original	1.6	0	0	0.229	0.362	1
	24 months after	0	3.4	88*	0.091	< 0.001#	< 0.001#
NYHA I-II class, %	original	0	1.1	0	0.402	1	0.447
	24 months after	32.8*	63.6*	82*	< 0.001	< 0.001	0.023
Sinus rhythm mainenance, %	original	0	0	0	1	1	1
	24 months after	4.9	65.9*	84*	< 0.001#	< 0.001#	0.022
LVIDd, cm	original	38.7	47.2	31.4	0.301	0.417	0.067
	24 months after	50.8*	87.5*	92.0*	< 0.001#	< 0.001#	0.414
LVIDs, cm	original	24.2	38.2	19.6	0.07	0.559	0.023
	24 months after	44.3*	72.7*	98*	< 0.001#	< 0.001#	< 0.001#
LVEDV, cm	original	21	21.3	11.8	0.955	0.193	0.154
	24 months after	36.1*	64.8*	66*	< 0.001#	< 0.001#	0.884
LVESV, cm	original	14.5	19.1	11.8	0.463	0.668	0.26
	24 months after	29.5*	64.8*	62*	< 0.001#	< 0.001#	0.745
LFEV, %	original	38.7	76.4	52.9	< 0.001#	0.13	0.004#
	24 months after	49.2*	81.8*	96*	< 0.001#	< 0.001#	0.018
RVD, cm	original	40.3	44.9	21.6	0.573	0.033	0.006#
	24 months after	68.9*	83*	96*	0.044	< 0.001#	0.03
LADs, cm	original	3.2	4.5	0	0.695	0.196	0.125
	24 months after	1.6	23.9*	48*	< 0.001#	< 0.001#	0.004#
RADs, cm	original	4.8	2.2	0	0.381	0.111	0.281
	24 months after	0	33*	54*	< 0.001#	< 0.001#	0.016#
PASP < 25 mmHg	original	0	0	0	1	1	1
	24 months after	3.3	34.1*	62*	< 0.001#	< 0.001#	0.002#

[a] Intergroup differences were calculated using Pearson's chi-square test or Fisher's exact test. The # sign indicates the required level of statistical significance, taking into account the Bonferroni correction.

[b] The statistical significance of repeated measures of qualitative traits was assessed using the McNemar test with Yates' correction.

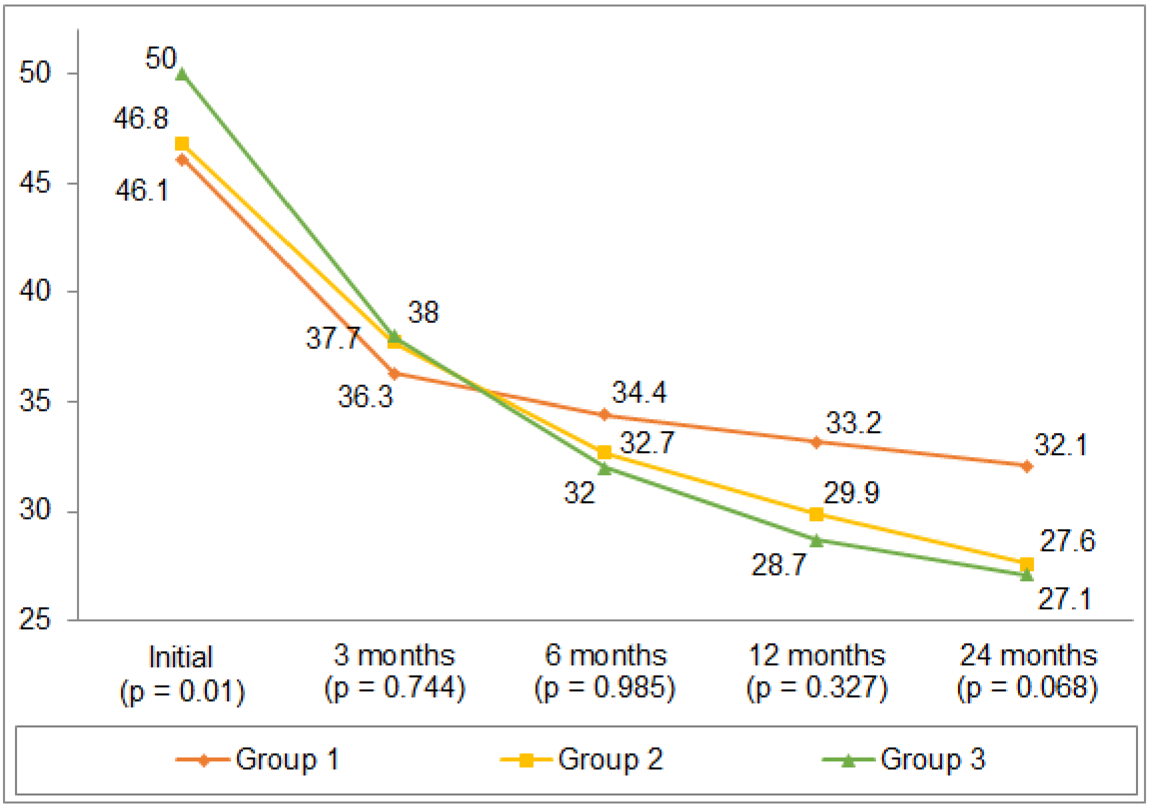

Fig. 2. Dynamics of pulmonary hypertension in patients of the studied groups

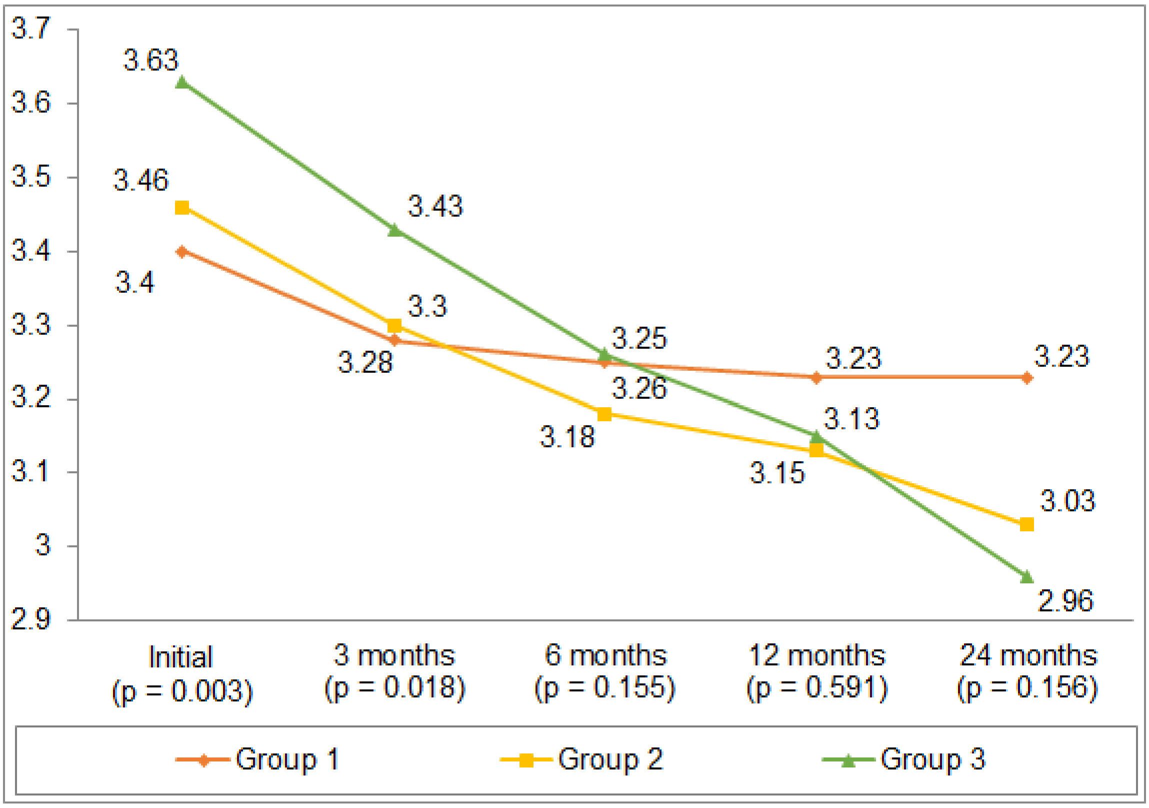

Fig. 3. Change in the size of the right ventricular cavity in patients of the studied groups

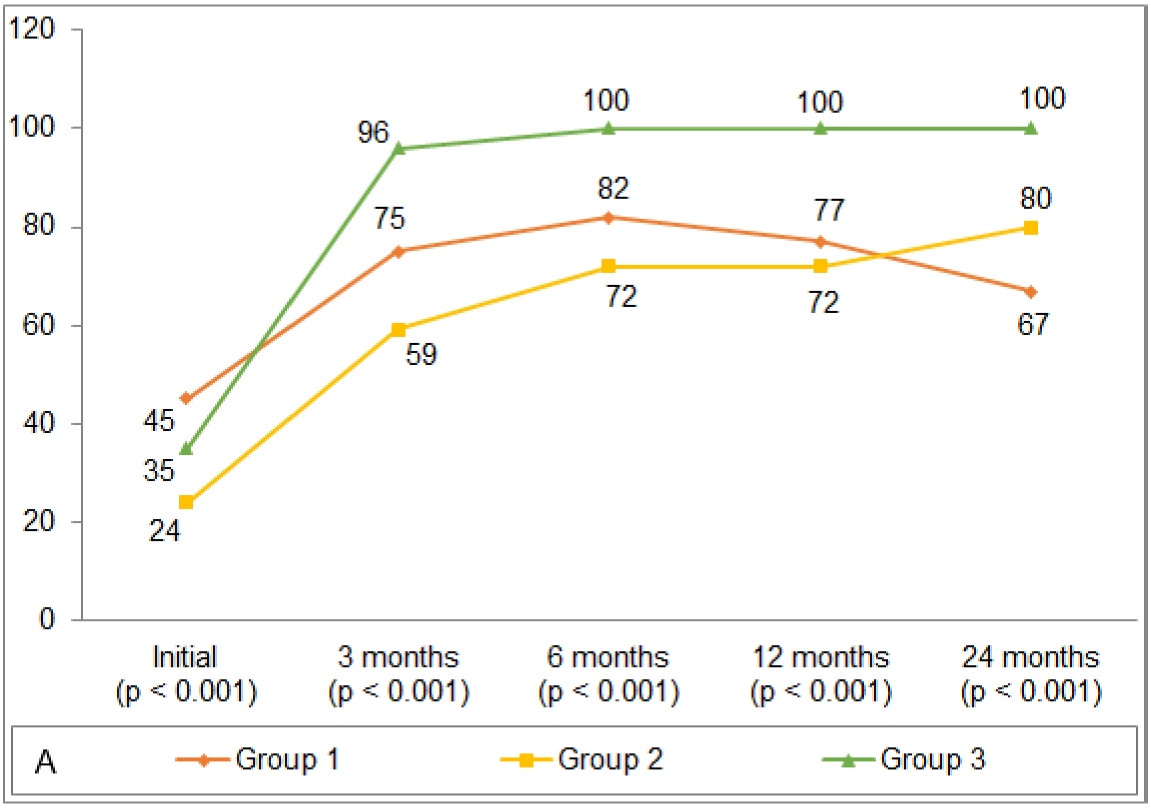

Fig. 4. Achievement of target values of tricuspid valve insufficiency (0-1) in the studied groups. Differences between the 3 groups were calculated using the chi-square test ($\chi 2$)

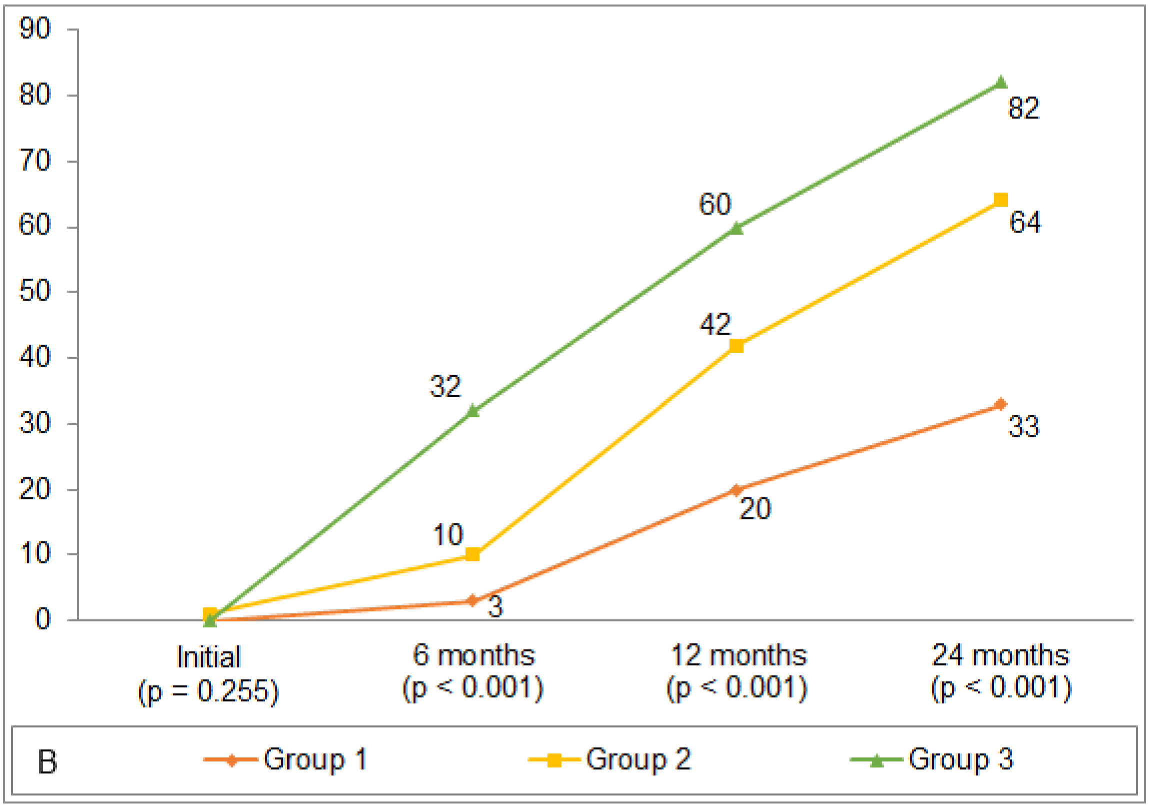

Fig. 5. Achievement of NYHA target heart failure class II in study groups

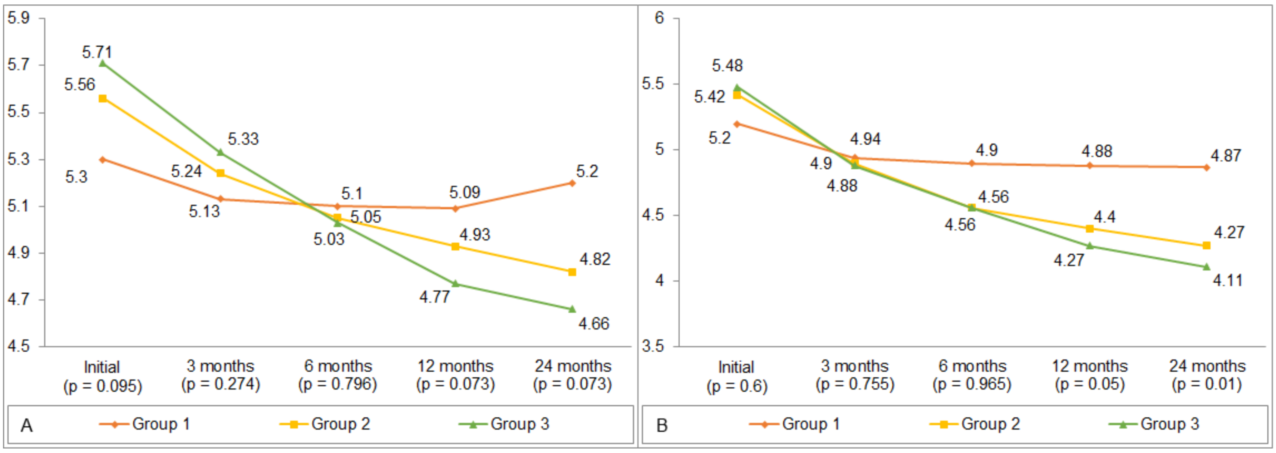

Fig. 6. Echocardiographic parameters of reverse cardiac remodeling: A – change in the size of the right atrium in the studied groups; B – change in the size of the left atrium in the study groups

Discussion

The study demonstrates the effectiveness of complex surgical correction in patients with mitral valve disease, AF and severe secondary PH, in which in addition to mitral valve and Maze IV surgery, circular PADN surgery was performed (Group 3). The control groups were initially comparable in terms of the main clinical and instrumental data, they also underwent surgery for mitral valve disease (Group 1) and simultaneous elimination of mitral valve disease and AF (Group 2), but patients in these groups did not receive specific surgical treatment of secondary PH. Even with a small number of examined patients and the absence of data on the effectiveness of the PADN procedure in the long-term period, the presented results demonstrate the best reverse cardiac remodeling, significant decrease in PH, restoration and maintenance of sinus rhythm in the postoperative period. Ultimately, the decrease in heart failure in patients of the 3rd group is more pronounced than in the control groups. The achieved result was obtained not only due to surgical correction of mitral valve disease and restoration of sinus rhythm after Maze IV, but also due to the circular PADN procedure.

The proposed method of surgical correction of PH was simple in terms of technical execution, did not take much time, and in the course of the research work proved to be absolutely safe. The result of our work was the demonstration of the effectiveness, practical significance and safety of the proposed technique.

No additional consumables were required for the PADN procedure, as the same AtriCure's Bipolar RF Clamps used for AF surgery was used. The use of a bipolar clamp-destructor makes it possible to carry out radiofrequency exposure along the entire circumference of the PA, which is advantageous compared to exposure only to the anterior wall of the trunk and orifices of the PA.

Based on the data obtained, the following conclusions can be drawn:

1. The PADN circular procedure is effective and safe, allows a significant decrease in the PH level in the postoperative period ($p\chi^2 = 0.018$ compared to the group without PADN) and promotes reverse cardiac remodeling.

2. Complex surgical correction of patients with mitral disease, AF and severe PH can significantly reduce heart failure ($p\chi^2 = 0.023$ compared to the group without PADN).

3. Further analysis of the effectiveness of radiofrequency denervation of the PA with the study of a larger number of patients, analysis of long-term results, and determination of the feasibility of this technique in patients with non-valvular forms of PH is needed.

Acknowledgements

Conflict of interest: none declared.

Funding statement: this work is supported by the Russian Science Foundation under grant 21-75-10075.

References

BABOKIN V. & TROFIMOV N. (2020): Prevention of Atrial Fibrillation Recurrence After the Maze IV Procedure. *The Annals of Thoracic Surgery* **109**, 1624-1625.

BAYLEN B.G., EMMANOUILIDES G.C., JURATSCH C.E., YOSHIDA Y., FRENCH W.J. & CRILEY J.M. (1980): Main pulmonary artery distention: a potential mechanism for acute pulmonary hypertension in the human newborn infant. *The journal of pediatrics* **96**, 540-4.

BRIONGOS FIGUERO S., MOYA MUR J.L., GARCIA-LLEDO A., CENTELLA T., SALIDO L., ACENA NAVARRO A. ET AL. (2016): Predictors of persistent pulmonary hypertension after mitral valve replacement. *Heart and vessels* **31**, 1091-1099.

CHEN S.L., ZHANG F.F., XU J., XIE D.J., ZHOU L., NGUYEN T. ET AL. (2013): Pulmonary artery denervation to treat pulmonary arterial hypertension: the single-center, prospective, first-in-man PADN-1 study (first-in-man pulmonary artery denervation for treatment of pulmonary artery hypertension). *Journal of the American college of cardiology* **62**, 1092-100.

GUAZZI M., VITELLI A., LABATE V. & ARENA R. (2012): Treatment for pulmonary hypertension of left heart disease. *Current treatment options in cardiovascular medicine* **14**, 319-27.

JURATSCH C.E., JENGO J.A., CASTAGNA J. & LAKS M.M. (1980): Experimental pulmonary hypertension produced by surgical and chemical denervation of the pulmonary vasculature. *Chest* **77**, 525-30.

OSORIO J. & RUSSEK M. (1962): Reflex changes on the pulmonary and systemic pressures elicited by stimulation of baroreceptors in the pulmonary artery. *Circulation research* **10**, 664-7.

TROFIMOV N.A., MEDVEDEV A.P., BABOKIN V.E. ET AL. (2009): Effect of circular sympathetic denervation of pulmonary arteries on the degree of pulmonary hypertension in patients with mitral valve pathology and atrial fibrillation. *Journal of clinical and experimental surgery* **4**, 32-41 (In Russian).

TROFIMOV N.A., MEDVEDEV A.P., NIKOLSKY A.V., KICHIGIN V.A., ZHAMLIKHANOVA S.S. & BABOKIN V.E. (2019): Denervation of Pulmonary Arteries in Patients with Mitral Valve Defects Complicated by Atrial Fibrillation and Pulmonary Hypertension. *Sovremennye tehnologii v medicine* **11**, 95-105 (In Russian).