УДК 616.126-089.844
DOI: https://doi.org/10.17816/mechnikov83711

Редукционная аннулопластика фиброзного кольца аутоперикардом при хирургическом лечении недостаточности митрального клапана

А.В. Сотников, М.В. Мельников, А.М. Битиева, Э.А. Колмаков

Северо-западный государственный медицинский университет им. И.И. Мечникова, Санкт-Петербург, Россия

Обоснование. Несмотря на широкое применение опорных колец при хирургическом лечении пациентов с недостаточностью митрального клапана и дилатацией его фиброзного кольца научные исследования в этой области продолжаются.

Цель исследования — изучить ближайшие и отдаленные результаты редукционной аннулопластики митрального клапана полоской из аутоперикарда расчетной длины.

Материалы и методы. В исследовании основную группу составил 21 пациент (средний возраст 60,9 ± 4,3 года, женщин — 23,8 %) с недостаточностью митрального клапана различного генеза с дилатацией фиброзного кольца. Сужение фиброзного кольца в ходе реконструкции клапана выполнили путем имплантации полоски из аутоперикарда расчетной длины по задним двум третям его окружности узловыми горизонтальными швами. Длина полоски рассчитана по оригинальной методике, согласно данным, полученным в ходе дооперационной чреспищеводной эхокардиографии, по формуле $2/3\pi \cdot D$ (мм), где D — существующая длина передней створки митрального клапана в срединной части от места прикрепления створки к фиброзному кольцу до свободного края в зоне сегмента А2. Контрольную группу составили 38 пациентов с недостаточностью митрального клапана неревматического генеза (средний возраст 59,1 ± 3,5 года, женщин — 23,7 %), у которых укрепление и сужение фиброзного кольца выполнили полоской из плетеного сосудистого протеза фиксированной длины 55 мм. В обеих группах помимо сужения фиброзного кольца также провели другие виды пластики клапана (шовную пластику створок, частичную резекцию створок, их комбинацию) и сочетанные процедуры (коронарное шунтирование, пластику постинфарктных аневризм левого желудочка).

Результаты. Подтверждена безопасность и надежность редукционной аннулопластики митрального клапана при аннулоэктазии. В сроки наблюдения до 8 лет (средний срок 3,5 ± 0,7 года) рецидивы значимой митральной регургитации с показаниями к повторной операции в обеих группах не зафиксированы. В основной группе пациентам выполнена более точная анатомическая коррекция клапана, чем в контрольной группе.

Выводы. В статье освещены существующие методы укрепления фиброзного кольца, их достоинства и недостатки. Предлагаемый способ редукционной аннулопластики митрального клапана полоской из аутоперикарда расчетной длины позволяет выполнить надежную и безопасную коррекцию расширенного фиброзного кольца при митральной недостаточности.

Ключевые слова: митральная регургитация; пластика митрального клапана; операция на открытом сердце; аннулоэктазия; аутоперикард.

Как цитировать:
Сотников А.В., Мельников М.В., Битиева А.М., Колмаков Э.А. Редукционная аннулопластика фиброзного кольца аутоперикардом при хирургическом лечении недостаточности митрального клапана // Вестник Северо-Западного государственного медицинского университета им. И.И. Мечникова. 2021. Т. 13. № 4. С. 53–64. DOI: https://doi.org/10.17816/mechnikov83711

Рукопись получена: 25.10.2021 **Рукопись одобрена:** 20.12.2021 **Опубликована:** 29.12.2021

ЭКО•ВЕКТОР

DOI: https://doi.org/10.17816/mechnikov83711

Reductive annuloplasty with autopericardium in surgical treatment of mitral insufficiency

Artem V. Sotnikov, Michail V. Melnikov, Anna M. Bitieva, Eduard A. Kolmakov

North-Western State Medical University named after I.I. Mechnikov, Saint Petersburg, Russia

BACKGROUND: Despite the widespread usage of all-type rings in the surgical treatment of patients with mitral valve insufficiency (MV) and dilatation of its fibrous annulus, the researches on this topic are in progress.

AIM: To study the short- and long-term results of narrowing annuloplasty of the MV utilizing an autopericardium strip of calculated length.

MATERIALS AND METHODS: The study group consisted of 21 patients (average age 60.9 ± 4.3 years, women 23.8 %) with MV insufficiency of non-rheumatic ethiology. The narrowing of the fibrous annulus during valve reconstruction has been performed along with the posterior 2/3 of their circle using interrupted horizontal sutures. With those sutures, an autopericardial strip of the calculated length has been secured to the annulus. The length of the strip has been calculated according to the original method, according to the data obtained during preoperative transesophageal echocardiography. The length of the strip was $2/3\pi \cdot D$ (mm), where D — the existing length of the anterior leaflet of the MV in the middle portion from the fibrous annulus to the free edge in the zone of the A2 segment. The control group consisted of 38 patients with non-rheumatic MV insufficiency (average age 59.1 ± 3.5 years, women 23.7 %); the strengthening and narrowing of the fibrous annulus have been performed using a strip made from a wicker vascular prosthesis. The length was 55 mm, equal for all the patients. In both groups, in addition to the narrowing of the fibrous annulus, other types of mitral valve-sparing surgery (partial resection of MV leaflets, suture leaflets techniques, their combination) and combined procedures (coronary bypass surgery, left ventricle reconstructions for postinfarction aneurysms) have been also performed.

RESULTS: In the studied groups, the safety and reliability of the performed restrictive MV annuloplasty procedures have been demonstrated. During the follow-up period up to 8 years (average 3.5 ± 0.7 years), there was no recurrence of significant mitral regurgitation, which would require repeated surgery in both groups. Narrowing annuloplasty of the fibrous annulus of MV with a strip from the autopericardium of an individual calculated length allows to perform a more accurate anatomical correction of the valve compared with the control group. The existing methods of mitral annuloplasty, their advantages and disadvantages are discussed.

CONCLUSIONS: The proposed method of restrictive annuloplasty of the MV with an autopericardial strip of the calculated length allows to perform a reliable and safe correction of the dilated fibrous annulus in patients with mitral insufficiency during valve-preserving operations.

Keywords: mitral regurgitation; mitral valve repair; open-heart surgery; annuloectasia; autopericardium.

To cite this article:
Sotnikov AV, Melnikov MV, Bitieva AM, Kolmakov EA. Reductive annuloplasty with autopericardium in surgical treatment of mitral insufficiency. *Herald of North-Western State Medical University named after I.I. Mechnikov.* 2021;13(4):53–64. DOI: https://doi.org/10.17816/mechnikov83711

Received: 25.10.2021 **Accepted:** 20.12.2021 **Published:** 29.12.2021

ECO•VECTOR

BACKGROUND

Mitral valve (MV) insufficiency is a common pathology that causes chronic heart failure (CHF) and impairs considerably quality of life. Hemodynamical MV insufficiency is one of the most common pathologies of the valvular apparatus of the heart among patients of the middle and older age groups, and affects 3.5% of people with ages over 65 years [11]. Dilatation of the annulus fibrosus (annulus ectasia) is associated with age-related changes in the MV and leads to impairment of cusp coaptation, loss of the obturator function, and the development of hemodynamical regurgitation. Dilatation of the MV annulus fibrosus often accompanies congenital subclinical pathology in the form of myxomatous changes in the valves, but as a rule, it clinically starts to manifest itself in middle and old ages.

Valve-preserving surgeries on the MV have undeniable advantages compared with prosthetics [17]. The choice of method for strengthening and narrowing the dilated annulus fibrosus in the complex surgical treatment of MV insufficiency is subject to further studies [6, 8, 10, 13, 14, 20].

This study aimed to analyze the immediate and long-term results of reductive annuloplasty of the annulus fibrosus using an autopericardial strip of the estimated length in the surgical treatment of MV insufficiency.

MATERIALS AND METHODS

Patients and Ethical Considerations

The study included 59 patients who underwent various types of plastic and reconstructive surgeries on the MV in combination with the correction of other structural pathologies of the heart in the Department of Cardiac Surgery and Surgical Treatment of Complex Arrhythmias and Cardiac Pacing of the I.I. Mechnikov North Western State Medical University from 2013 to 2021.

Surgical Procedures

Reductive annuloplasty of the MV fibrous annulus with an autopericardial strip was performed during combined interventions on the MV in 21 patients (main group). The control group consisted of 38 patients. In these patients, a fixed length strip of 55 mm from a braided synthetic vascular

Table 1. Clinical characteristics of the studied patients groups
Таблица 1. Клиническая характеристика изучаемых групп пациентов

Clinical characteristics	Patient groups		Level of significance *p*
	main (*n* = 21)	control (*n* = 38)	
Average age, years	60.9 ± 4.3	59.1 ± 3.5	>0.05
Female gender, *n* (%)	5 (23.8)	9 (23.7)	>0.05
Grade II–III hypertension, *n* (%)	13 (61.9)	25 (65.8)	>0.05
Ischemic heart disease, *n* (%)	8 (38.1)	16 (42.1)	>0.05
Diabetes mellitus, *n* (%)	6 (28.6)	10 (26.3)	>0.05
Chronic obstructive pulmonary disease, *n* (%)	2 (9.5)	3 (7.9)	>0.05
Atrial fibrillation, *n* (%)	11 (52.4)	14 (36.8)	>0.05
Grade I CHF, *n* (%)	0	0	>0.05
Grade II CHF, *n* (%)	4 (19.0)	11 (28.9)	>0.05
Grade III CHF, *n* (%)	15 (71.4)	24 (63.2)	>0.05
Grade IV CHF, *n* (%)	2 (9.6)	3 (7.9)	>0.05
Mean value of CHF grade	2.9 ± 0.2	2.8 ± 0.2	>0.05
Echocardiography data			
Hemodynamically MV insufficiency, *n* (%)	21 (100.0)	38 (100.0)	>0.05
Left ventricular ejection fraction, %	59.7 ± 4.6	55.5 ± 5.3	>0.05
Diastolic dimension of the left ventricle, mm	56.1 ± 3.6	56.9 ± 1.9	>0.05
Left atrium size, mm	48.4 ± 3.3	43.8 ± 2.3	0.03
Diameter of MV annulus fibrosus (normal up to 30–35 mm [1]), mm	39.1 ± 3.1	37.6 ± 2.4	>0.05
Pulmonary artery pressure, mm Hg	53.9 ± 7.4	47.4 ± 4.4	>0.05

Note: MV — mitral valve, CHF — chronic heart failure.

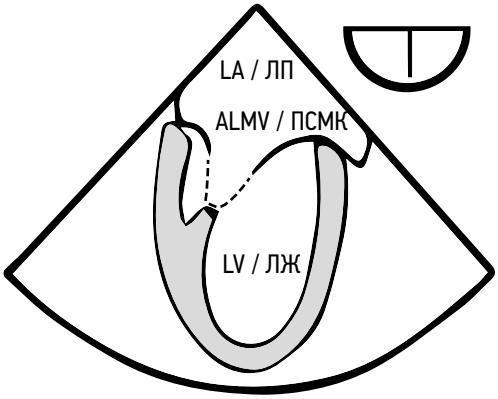

Fig. 1. Schematic illustration of a two-chamber plane of the heart when performing transesophageal echocardiography, necessary to determine the length of the median part of the anterior mitral valve leaflet: the measurement is carried out from the fibrous annulus to the free edge of the leaflet in the A2 segment. LV — left ventricle, LA — left atrium, ALMV — the anterior leaflet of the mitral valve
Рис. 1. Схема двухкамерной проекции сердца при выполнении чреспищеводной эхокардиографии, необходимой для определения длины срединной части передней створки митрального клапана: измерение от фиброзного кольца до свободного края створки в сегменте А2. ЛЖ — полость левого желудочка, ЛП — полость левого предсердия, ПСМК — передняя створка митрального клапана

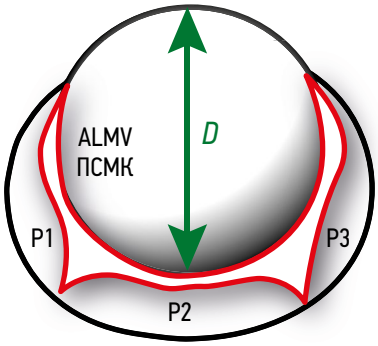

Fig. 2. Mitral valve. Viewed from the operator's side. There is a dilation of the fibrous annulus; the cusps do not close; lengthening of the P2 segment of the posterior cusp. Diagram of the anterior mitral valve leaflet: *D* — target fibrous annulus diameter after implantation of an autopericardial strip; ALMV — the anterior leaflet of the mitral valve; P1, P2, P3 — segments of the posterior leaflet of the mitral valve
Рис. 2. Митральный клапан. Вид со стороны оператора. Дилатация фиброзного кольца, створки не смыкаются, удлинение сегмента Р2 задней створки. Схема участка передней створки митрального клапана: *D* — целевой диаметр фиброзного кольца после имплантации полоски из аутоперикарда; ПСМК — передняя створка митрального клапана; Р1, Р2, Р3 — сегменты задней створки митрального клапана

prosthesis 5 mm wide was used for reductive annuloplasty of the MV. Some of the clinical characteristics of the patients are listed in Table 1. The main cause of the development of mitral regurgitation in patients in both studied groups was myxomatous degeneration of the MV cusps or a combination of this pathology with coronary heart disease. Patients with mitralization of aortic valve defects and MV lesions of rheumatic origin were excluded from the analysis. Despite the mitral insufficiency, the patients had a common symptom, namely dilatation of the MV annulus fibrosus. All surgeries were performed by a single surgeon, and included median sternotomies and cardiopulmonary bypass, cardioplegia, and moderate hypothermia.

The two groups of patients were comparable in terms of the main clinical and echocardiographic characteristics. At their ages (approximately 60 years), MV bioprosthetics was not recommended. The prevalence of comorbidities in the groups did not differ considerably. Various forms of atrial fibrillation, from paroxysmal to permanent, were verified in almost half of the main group patients and in a third of patients in the control group. According to echocardiography, hemodynamical MV insufficiency (confirmed by the presence

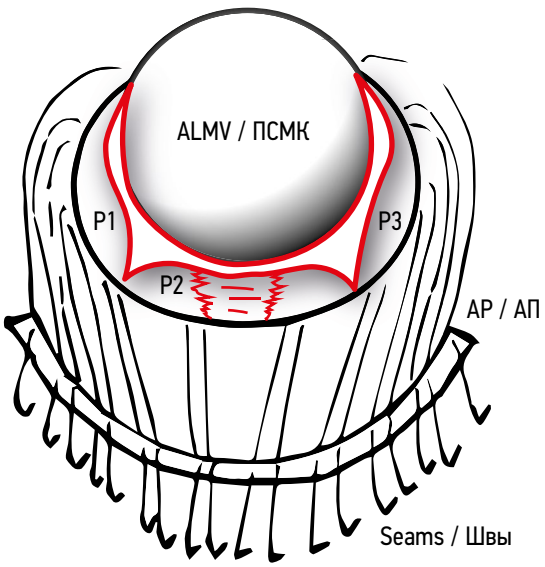

Fig. 3. Sutured mitral annulus and sutured autopericardial strip. The width of the strip is 5 mm; the length of the strip is calculated according to the formula. On the fibrous ring of the mitral valve, single horizontal sutures from a braided synthetic thread 2/0 are imposed, which are then sutured through a strip of autopericardium. Valvuloplasty in the form of resection of the lengthened P2 segment of the posterior leaflet of the MV is presented as an example of simultaneous intervention on the valves. ALMV — the anterior leaflet of the mitral valve; P1, P2, P3 — segments of the posterior leaflet of the mitral valve; AP — a strip from the autopericardium
Рис. 3. Прошитое фиброзное кольцо митрального клапана и прошитая полоска из аутоперикарда. Ширина полоски 5 мм, длина полоски рассчитана по формуле. На фиброзное кольцо митрального клапана наложены одиночные горизонтальные швы из плетеной синтетической нити 2/0, которые затем прошиты через полоску из аутоперикарда. В качестве примера одновременного вмешательства на створках приведена вальвулопластика в виде резекции удлиненного сегмента Р2 задней створки митрального клапана. ПСМК — передняя створка митрального клапана; Р1, Р2, Р3 — сегменты задней створки митрального клапана; АП — полоска из аутоперикарда

of pulmonary hypertension) with a slightly reduced left ventricular ejection fraction, in conjunction with initial dilatation, expansion of the MV annulus, and atriomegaly, were diagnosed in both groups. We associated a more pronounced development of atriomegaly in patients of the main group with prolonged records of mitral regurgitation.

Reductive annuloplasty with an autopericardial strip has been performed in our clinic since November 2018. This strip is formed from the anterior pericardium accessed after opening the thoracic cavity. The individual calculation of the autopericardial strip length for each patient (application for invention 2021123942 dated August 12, 2021) was characterized by the correction of the expanded MV annulus fibrosus in the main group. The target fibrotic annulus circumference was calculated from the size of the anterior MV cusp as determined by transesophageal echocardiography. Immediately before the onset of surgery, the MV was visualized in a two-chamber projection to observe the anterior cusp movement in cross section (Fig. 1). Subsequently, the length of the median part of the anterior MV cusp was measured in systole from its base near the annulus fibrosus to the free edge in the A2 segment (Fig. 2). This initial length of the anterior cusp was used as the target diameter of the MV annulus fibrosus (Figs. 3 and 4).

The autopericardial strip length was calculated by the formula $l = 2.1 \times D$, where l is the target length of the formed strip, 2.1 is a constant coefficient equal to $2/3\pi$ (where $\pi \approx 3.14$), and D is the initial length of the median part of the anterior MV cusp from the annulus fibrosus to the free margin in the area of the A2 segment. That is, the strip length for correction should be 53 mm with an anterior cusp length of 25 mm, 63 mm with a cusp length of 30 mm, 74 mm with a cusp length of 35 mm, 84 mm with a cusp length of 40 mm, and 95 mm with a cusp length of 45 mm, respectively. The strips were implanted with interrupted n-shaped sutures with a 2/0 synthetic braided suture, applied on the MV fibrous annulus along the posterior two thirds of its circumference

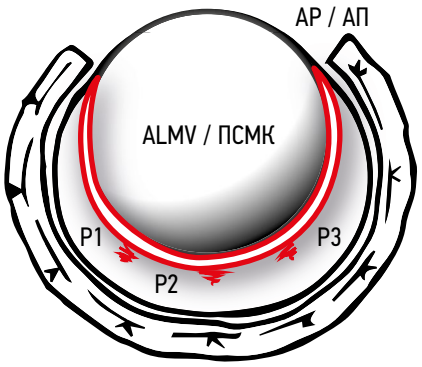

Fig. 4. An autopericardial strip is implanted; the interrupted sutures are tied. The final view of the mitral valve after correction of the concomitant pathology of the posterior leaflet (in this case, resection of the segment P2 of the posterior leaflet) and narrowing of the dilated fibrous annulus by implantation of a strip from the autopericardium of the estimated length. ALMV — the anterior leaflet of the mitral valve; P1, P2, P3 — segments of the posterior leaflet of the mitral valve; AP — a strip from the autopericardium
Рис. 4. Полоска из аутоперикарда имплантирована, узловые швы завязаны. Окончательный вид митрального клапана после коррекции сопутствующей патологии задней створки (в данном случае резекции сегмента задней створки P2) и сужения расширенного фиброзного кольца имплантацией полоски из аутоперикарда расчетной длины. ПСМК — передняя створка митрального клапана; P1, P2, P3 — сегменты задней створки митрального клапана; АП — полоска из аутоперикарда

Table 2. Full range of performed open heart surgeries
Таблица 2. Полный объем вмешательств на сердце

Clinical characteristics	Patient groups		Level of significance *p*
	main (*n* = 21)	control (*n* = 38)	
Isolated reductive annuloplasty of MV, *n* (%)	3 (14.3)	17(44.7)	0.02
Combination of reductive annuloplasty with valvuloplasty			
Resection of a segment of the posterior MV cusp with annuloplasty, *n* (%)	12 (57.1)	14 (36.8)	>0.05
MV suture grafting with annuloplasty, *n* (%)	5 (23.8)	2 (5.3)	0.03
Cusp segment resection with MV suture grafting and annuloplasty, *n* (%)	1 (4.8)	5 (13.1)	>0.05
Concomitant correction of other cardiac pathology			
Resection of the left atrial appendage in patients with atrial fibrillation, *n* (%)	11 (52.4)	14 (36.8)	>0.05
Coronary bypass surgery, *n* (%)	8 (38.1)	16 (42.1)	>0.05
Tricuspid valve correction, *n* (%)	3 (14.3)	4 (10.5)	>0.05
Grafting of postinfarction aneurysm of the left ventricle, *n* (%)	1 (4.8)	3 (7.9)	>0.05

Note: MV — mitral valve.

with a transition to the areas of both commissures. Typically, 7–9 sutures were applied after correction of the pathology of the cusps or subvalvular apparatus (resection of a posterior cusp segment, various types of suture repairs, and combinations thereof) (Table 2).

Table 2 demonstrates the full scope of interventions on the heart. In reconstructive valve-sparing surgeries on the MV with dilatation of the annulus fibrosus, the procedures were rarely limited to isolated annuloplasty (14.7% in the main group versus 44.7% in the control group ($p < 0.05$)). Most patients underwent additional correction of both MV cusps (resection of segments, suture plasty, or their combination), as well as for other cardiac pathologies (coronary, valvular, or combined).

After completing the main stage of the surgery and the subsequent (mandatory) procedures to restore effective cardiac activity, control transesophageal echocardiography was performed. After annuloplasty in the control group, emergency mitral valve replacement due to anterior systolic MV cusp movement (SAM syndrome) was required in two patients. There were no such patients in the main group.

To prevent wound complications, we have been using an effective method of combined (systemic and local) prevention of postoperative sternomediastinitis with cefazolin [5] since 2014. Our efficiency associated with the successful completion of this method has been proven in practice. From the first day of the postoperative period, warfarin was prescribed to the patients according to existing standards up to the target values of the international normalized ratio with values in the range of 2.0–3.0. Six months after the surgery, warfarin was discontinued. In the presence of atrial fibrillation, treatment with direct anticoagulants (rivaroxaban, apixaban, or dabigatran etexilate) was continued throughout their lives.

RESULTS

The efficiency of the proposed method of MV annuloplasty was evaluated comparatively according to the main characteristics of the course of the early postoperative period (Table 3).

By the time of discharge from the hospital, positive trends were recorded in both groups according to echocardiography compared with preoperative values. Specifically, significant decreases in the sizes of the left chambers of the heart were noted (in the main group, decreases in the size of the left atrium from 48.4 ± 3.3 (mean ± standard deviation) to 43.1 ± 2.7 mm, and diastolic size of the left ventricle from 56.1 ± 3.6 to 53.3 ± 2.6 mm were documented; in the control group, the respective changes were from 43.8 ± 2.3 to 40.9 ± 1.8 mm and from 56.9 ± 1.9 to 49.9 ± 3.4 mm), while pressure indicators approached the norm values (from 53.9 ± 7.4 to 36.2 ± 3.6 mm Hg in the main group, and from 47.4 ± 4.4 to 36.5 ± 2.7 mm Hg in the control group). These data indicate the efficiency of the MV correction and other structural cardiac pathologies (coronary and/or valvular) in both groups. Patients of the main group had a shorter duration of postoperative mechanical ventilation of the lungs and stay in the intensive care unit. We attribute this fact to changes in the approaches used to treat cardiac patients in the intensive care unit of our clinic in recent years.

In the main group, there was a significantly lower incidence of MV insufficiency above grade II, according to echocardiography data (9.5% versus 31.6%), and a significantly lower mean pressure gradient (2.5 versus 3.6 mm Hg) than that in the control group. For patients with moderate MV insufficiency, we provided yearly follow-ups with check-ups based on echocardiography and heart failure grade assessments using the 6-min walk test. During the optimal drug therapy in these patients, there was no indication for the need of repeated surgery. In our opinion, the main reason for the higher incidence of moderate MV insufficiency in the control group is the use of a fixed length strip for annuloplasty.

Despite the hemodynamically insignificant indicators of the average pressure gradient, a significant difference in the groups indicates that individual selection of the strip length for narrowing the annulus fibrosis of the MV allows more accurate anatomical correction in patients with annulodilatation.

Manifestations of systemic inflammation in the early postoperative period in the main group were also less pronounced than those in the control group according to the control clinical blood test. Specifically, significantly lower levels of leukocytes (8.0 ± 1.3 versus 9.4 ± 1.0 × 10^9/L), platelets (246.8 ± 39.9 vs. 307.7 ± 31.7 × 10^9/L), C-reactive protein (29.6 ± 7.4 vs. 63.4 ± 18.8 mg/L), eosinophils (0.3 ± 0.0 vs. 0.4 ± 0.1 × 10^9/L), thrombocrit (0.2 ± 0.0 vs. 0.3 ± 0.0 × 10^2/L), percentage distribution of platelets by volume (17.0 ± 0.3 vs. 16.4 ± 0.1%), and absolute neutrophil count (5.2 ± 1.1 vs. 6.3 ± 0.8 × 10^9/L).

In the early postoperative period, one control group patient, who was in a serious condition at the beginning of the study, died. The cause of death was the progression of heart failure after surgery, which included left ventricular thrombectomy, resection of postinfarction aneurysm, left ventricular repair, coronary bypass grafting, and combined MV repair. The rest of the patients were discharged on days 10–12 after their surgeries if they exhibited satisfactory conditions following outpatient management by a cardiologist at the primary healthcare facility.

The long-term results of the study were analyzed in 33 control group patients and in 19 main group patients. The maximum follow-up period was 8 years, and the average follow-up period was 3.5 ± 0.7 years. The methods of examination included telephone surveys with a modified

Table 3. Brief characteristics of the early postoperative period according to the clinical, laboratory tests, and instrumental control

Таблица 3. Краткая характеристика раннего послеоперационного периода, по данным клинического, лабораторного и инструментального контроля

Clinical characteristics	Patient groups		Level of significance *p*
	main (*n* = 21)	control (*n* = 38)	
Average amount of drainage discharge in the postoperative period, mL	410 ± 140	480 ± 180	>0.05
Number of patients requiring donor blood transfusion, *n* (%)	4 (19.0)	8 (21.0)	>0.05
Duration of postoperative artificial lung ventilation, h	3.1 ± 1.3	5.3 ± 1.3	0.045
Duration of stay in the intensive care unit, days	1.7 ± 0.2	2.3 ± 0.4	0.02
Acute renal failure in the postoperative period, *n* (%)	2 (9.5)	4 (10.5)	>0.05
Acute cerebrovascular accident in the early postoperative period, *n* (%)	1 (4.7)	1 (2.6)	>0.05
Hospital mortality, *n* (%)	0 (0)	1 (2.6)	>0.05
Echocardiography data 7–10 days after surgery			
Left ventricular ejection fraction, %	57.6 ± 5.3	53.3 ± 6.0	>0.05
Left atrium size, mm	43.1 ± 2.7	40.9 ± 1.8	>0.05
Diastolic dimension of the left ventricle, mm	53.3 ± 2.6	49.9 ± 3.4	>0.05
Pulmonary artery pressure, mm Hg	36.2 ± 3.6	36.5 ± 2.7	>0.05
Moderate MV insufficiency, *n* (%)	2 (9.5)	12 (31.6)	0.05
Average pressure gradient on the MV, mm Hg	2.5 ± 0.5	3.6 ± 0.7	0.04
Indicators of a clinical blood test on days 7–10 after surgery			
Leukocyte count, $\times 10^9$/L	8.0 ± 1.3	9.4 ± 1.0	0.045
Platelet count, $\times 10^9$/L	246.8 ± 39.9	307.7 ± 31.7	0.009
Mean platelet volume, fL	8.5 ± 0.5	8.6 ± 0.4	>0.05
Plateletcrit, $\times 10^2$/L	0.2 ± 0.0	0.3 ± 0.0	0.009
Platelet distribution volume, %	17.0 ± 0.3	16.4 ± 0.1	0.0007
Neutrophils, total, %	62.8 ± 3.7	65.8 ± 2.9	>0.05
Lymphocytes, %	22.6 ± 3.6	20.1 ± 2.3	>0.05
Monocytes, %	10.4 ± 1.0	9.6 ± 0.9	>0.05
Eosinophils, %	3.6 ± 0.7	4.1 ± 0.8	>0.05
Basophils, %	0.6 ± 0.2	0.4 ± 0.2	>0.05
Neutrophils, absolute count, $\times 10^9$/L	5.2 ± 1.1	6.3 ± 0.8	0.03
Lymphocytes, absolute count, $\times 10^9$/L	1.7 ± 0.2	1.9 ± 0.2	>0.05
Monocytes, absolute count, $\times 10^9$/L	0.8 ± 0.2	0.9 ± 0.1	>0.05
Eosinophils, absolute count, $\times 10^9$/L	0.3 ± 0.0	0.4 ± 0.1	0.03
C-reactive protein (normal 0–5 mg/L), mg/L	29.6 ± 7.4	63.4 ± 18.8	0.002

Note: MV — mitral valve.

CROQ questionnaire [22], case outpatient follow-ups of the patients, and control echocardiography for patients with moderate MV insufficiency in six months, one year, and in every subsequent year following surgeries.

In the long-term period, the majority of patients in both groups evaluated positively the surgical treatment and noted high tolerance to physical activity. In total, 84.2% of patients in the main group and 63.6% in the control group lead an active lifestyle. Several patients were employed and were engaged in fitness programs.

The severity of CHF in patients of both groups in the long-term period is presented in Table 4. Patients with grade II CHF experienced minor limitations in physical activity during heavy physical exertion, and noted swelling of the lower extremities.

Table 4. Severity of chronic heart failure in the long-term period after surgery

Таблица 4. Выраженность хронической сердечной недостаточности в отдаленном периоде после операции

Clinical characteristics	Patient groups		Level of significance *p*
	main (*n* = 19)	control (*n* = 33)	
Average time after surgery, years	1.3 ± 0.6	4.6 ± 0.7	0.015
Grade I CHF, *n* (%)	16 (84.2)	21 (63.6)	>0.05
Grade II CHF, *n* (%)	3 (15.8)	10 (30.3)	>0.05
Grade III CHF, *n* (%)	0	2 (6.1)	>0.05
Grade IV CHF, *n* (%)	0	0	>0.05
Average value of CHF grade	1.1 ± 0.2	1.4 ± 0.2	0.03

Note: CHF — chronic heart failure.

A slight increase in diuretic therapy on an outpatient basis enabled us to arrest the edematous syndrome and improve the general conditions of these patients.

In the main group, two patients were diagnosed with grade III CHF. In case 1, severe CHF was caused by an initially disabled left ventricle associated with a postinfarction heart aneurysm. She was admitted to our clinic in an orthopnea position and with dyspnea symptoms at rest. After stabilization of her condition, she underwent resection of the postinfarction aneurysm and combined left ventricular grafting supplemented by reductive MV annuloplasty. The patient was discharged after surgery in 2015 with physical exertion tolerance classified as grade II CHF. However, over the past few years, she has noted an exacerbation of dyspnea. Echocardiography showed no remarkable MV insufficiency, however reduced myocardial contractility and a left ventricular ejection fraction less than 30% were revealed. Patient 2 was suspected to have recurrent mitral regurgitation. According to fibrogastroscopy, a giant hiatus hernia squeezed the cavity of the left atrium from the outside and deformed the MV annulus fibrosus. The patient still refuses the proposed diaphragmatic hernia repair that is necessary to allow the re-evaluation of the MV function.

There were no recurrences of remarkable MV insufficiency with the development of grade IV CHF and indications for re-intervention in both groups.

The average follow-up period in the main group was significantly less than that of the control group. This was due to the design of our study, which was a prospective, non-randomized study with a continuous sample of patients. Despite this difference, we believe that the comparison of these groups of patients is acceptable given that our experience and the data from other authors have proven that one year after surgery, the results remain stable for a few years [21, 27].

The follow-up revealed that in some cases, severe CHF may develop owing to the appearance of atrial flutter in the long term, when patients can hardly tolerate heart rates higher than 150 beats per minute. Three patients admitted to the clinic at different times after MV grafting with suspected recurrence of severe MV insufficiency noted pronounced manifestations of grade IV CHF. During the examination, these patients were diagnosed with a permanent form of atrial flutter with a high-heart rate manifested 0.5–1.5 years after the surgery. Sinus rhythm was restored by defibrillation in one case, and by endovascular radiofrequency ablation of the arrhythmogenic zones of the right atrium in two other patients. Further intensification of CHF therapy according to existing standards enabled us to discharge these patients with grade II CHF. According to transesophageal echocardiography, they had moderate MV insufficiency without any indications for repeated surgery.

The results of the follow-ups of patients after surgery indicated the reliability of the MV annuloplasty technique with strips from synthetic braided material and the autopericardium. However, in the main group, a trend toward a more favorable course of the postoperative period was revealed with a greater number of patients with grade I CHF, and a significantly lower ($p < 0.05$) average value of the CHF grade in the main group compared with the control group.

DISCUSSION

The choice of method for strengthening and narrowing the annulus fibrosus of the MV during valve-sparing surgeries in patients with mitral regurgitation is subject to further study [6, 8, 10, 13, 14, 20]. Implantation of supporting synthetic rings is used most commonly. This method was proposed by Carpentier in the 1970s, and has been used all over the world for more than 40 years. The choice of the ring size and the method of its implantation were repeatedly described in the literature, and the immediate and long-term results were studied in detail. One of the main disadvantages of this method is the rigid fixation of the MV annulus fibrosus, which excludes its participation in the function of the heart [19, 24]. The diameter and shape of the MV annulus fibrosus are known to be constantly changing at different phases of the cardiac cycle [15, 24]. Therefore its fixation with a rigid

support ring can reduce the MV functionality and increase the incidence of SAM syndromes [25].

An alternative to this method is the strengthening and narrowing of the MV annulus fibrosus using flexible half rings [13], synthetic strips [6], and implant-free suture techniques [8]. Despite their proven efficiency, these methods also have disadvantages. In particular, suture techniques can be unreliable in the long-term period and often lead to relapses of significant hemodynamical MV insufficiency (up to 22.9% of cases at a mean follow-up of 2.4 ± 0.8 years) [3]. The use of flexible half rings or synthetic strips involves the implantation of foreign material into the cardiac cavity, which can activate the immune system with the development of local and systemic inflammation and local thrombogenesis [18].

Most of these shortcomings can be avoided by using the patient's own tissues as a reinforcing material for MV reductive annuloplasty, such as the autopericardial strip proposed for grafting in 1991 [20]. This method allows the preservation of the functionality of the MV annulus fibrosus without its rigid fixation [16, 23]. This is important for physically active patients [26], but also avoids immune system activation and the development of an inflammatory reaction. Long-term results provide evidence to the reliability of mitral annuloplasty with the use of the autopericardium, whereby the incidence of significant hemodynamical recurrences of MV insufficiency in the follow-up period up to 5 years is 2.9% [27], but it does not exceed 14% after 15 years [21].

The issue pertaining to the optimal length of the strip for the necessary narrowing of the dilated MV annulus fibrosus has not yet been resolved. Most research authors use a fixed-strip length [4, 9, 12, 14, 20]. At the same time, it is obvious that it does not correspond to the individual characteristics of the valvular apparatus of each patient. Most often, the strip length is determined by the operating surgeon based on his experience and patient case specifics, which can result in errors. Insufficient narrowing of the annulus fibrosus does not ensure complete restoration of the obturating function of the MV, and excessive narrowing can lead to the development of relative MV stenosis or SAM syndrome [7]. To our knowledge, this is the first time a method is proposed for calculation of the autopericardial strip length on a per-patient case basis depending on the initial size of the MV structures during reductive annuloplasty of the dilated annulus fibrosus. Some authors suggested the use of the length of the posterior MV semicircle to individualize the length of the autopericardial strip [2]. However, this method can be used only in the absence of dilatation of the MV annulus fibrosus when the aim of the surgery is not the reduction of its diameter.

The existing methods of reductive annuloplasty used in the correction of dilatation of the MV's annulus fibrosus, including the use of the autopericardium, are not free from shortcomings, and continue to lead to disputes. The proposed method used for narrowing the annulus fibrosus with a calculated strip length from the autopericardium in patients with mitral insufficiency of nonrheumatic origin enables the performance of more accurate anatomical corrections of the MV. At the same time, the annulus fibrosus retains its elasticity and functionality as evidenced by the long-term results of the study.

CONCLUSIONS

1. The method of reductive MV annuloplasty with an autopericardial strip of an individually selected length enables the performance of reliable and safe narrowing of the annulus fibrosus in patients with MV insufficiency when performing valve-preserving surgeries.
2. The proposed formula for calculating the autopericardial strip length in patients with annulus ectasia enables the individualization of the MV reductive annuloplasty method and the accurate calculation of the required narrowing of the annulus fibrosus.

ADDITIONAL INFORMATION

Funding. The study received no external funding.

Conflict of interest. The authors declare no conflicts of interest.

All authors made considerable contributions to the study and preparation of the article, and read and approved the final version before its publication.

REFERENCES

1. Bockeria LA, Mashina TV, Dzhanketova VS, Golukhova EZ. Ultrasound anatomy and three-dimensional transesophageal echocardiography in mitral valve surgery (review). *Creative cardiology.* 2014;8(4):65–75. (In Russ.)

2. Patent RU 2740122C1/11.01.2021. Vajkin VE, ZHurko SA, Pimenova PV, et al. Method for mitral valve plasty of an autopericardial band in ischemic mitral insufficiency. (In Russ.)

3. Gordeev ML, Maistrenko AD, Sukhova IV, et al. Suture annuloplasty for surgical treatment of ischemic mitral regurgitation: long-term results. *Pathology of blood circulation and cardiac surgery.* 2015;19(1):36–42. (In Russ.). DOI: 10.21688/1681-3472-2015-1-36-42

4. Patent RU 2679870C1/13.02.2019. Lishchuk AN, Koltunov AN, Esion GA, Karpenko IG. Sposob plastiki priobretennogo poroka mitral'nogo klapana. (In Russ.)

5. Patent RU 2707262C1/25.11.2019. Sotnikov AV, Mel'nikov VM, El'madzhi RV. Sposob profilaktiki posleoperacionnogo perednego mediastinita posle vypolneniya polnoj prodol'noj sternotomii pri otkrytyh operaciyah na serdce. (In Russ.)

6. Shneider YuA, Talipov IR, Uzhakhov IR. Changes of intracardiac hemodynamics in plasty of the mitral valve with a synthetic band, early period of observation. *Grekov's Bulletin of Surgery.* 2011;170(5):54–56. (In Russ.)
7. Alfieri O, Lapenna E. Systolic anterior motion after mitral valve repair: where do we stand in 2015? *Eur J Cardiothorac Surg.* 2015;48(3):344–346. DOI: 10.1093/ejcts/ezv230
8. Barlow CW, Ali ZA, Lim E, et al. Modified technique for mitral repair without ring annuloplasty. *Ann Thorac Surg.* 2003;75(1):298–300. DOI: 10.1016/s0003-4975(02)03924-3
9. Brown ML, Schaff HV, Li Z, et al. Results of mitral valve annuloplasty with a standard-sized posterior band: is measuring important? *J Thorac Cardiovasc Surg.* 2009;138(4):886–891. DOI: 10.1016/j.jtcvs.2009.01.022
10. Bruno VD, Di Tommaso E, Ascione R. Annuloplasty for mitral valve repair in degenerative disease: to be flexible or to be rigid? That's still the question. *Indian J Thorac Cardiovasc Surg.* 2020;36(6):563–565. DOI: 10.1007/s12055-020-01001-3
11. Cahill TJ, Prothero A, Wilson J, et al. Community prevalence, mechanisms and outcome of mitral or tricuspid regurgitation. *Heart.* 2021;107(12):1003–1009. DOI: 10.1136/heartjnl-2020-318482
12. Calafiore AM, Di Mauro M, Gallina S, et al. Optimal length of pericardial strip for posterior mitral overreductive annuloplasty. *Ann Thorac Surg.* 2003;75(6):1982–1984. DOI: 10.1016/s0003-4975(02)04685-4
13. Gillinov AM, Cosgrove DM3rd, Shiota T, et al. Cosgrove-Edwards Annuloplasty System: midterm results. *Ann Thorac Surg.* 2000;69(3):717–721. DOI: 10.1016/s0003-4975(99)01543-x
14. Hetzer R, Delmo Walter EM. No ring at all in mitral valve repair: indications, techniques and long-term outcome. *Eur J Cardiothorac Surg.* 2014;45(2):341–351. DOI: 10.1093/ejcts/ezt322
15. Nishi H, Toda K, Miyagawa S, et al. Annular dynamics after mitral valve repair with different prosthetic rings: A real-time three-dimensional transesophageal echocardiography study. *Surg Today.* 2016;46(9):1083–1090. DOI: 10.1007/s00595-015-1279-z
16. Omay O, Ozker E, Indelen C, et al. Posterior pericardial annuloplasty in ischemic mitral regurgitation. *Heart Surg Forum.* 2009;12(5):E285–290. DOI: 10.1532/HSF98.20091006
17. Onorati F, Santini F, Dandale R, et al. Functional mitral regurgitation: a 30-year unresolved surgical journey from valve replacement to complex valve repairs. *Heart Fail Rev.* 2014;19(3):341–358. DOI: 10.1007/s10741-013-9392-9
18. Padang R, Ali YZ, Mankad R, et al. Thromboembolic complications of annuloplasty rings. *JACC Cardiovasc Imaging.* 2021;14(8):1659–1665. DOI: 10.1016/j.jcmg.2020.08.038
19. Roshanali F, Vedadian A, Shoar S, et al. The viable mitral annular dynamics and left ventricular function after mitral valve repair by biological rings. *Int Cardiovasc Res J.* 2012;6(4):118–123.
20. Salati M, Scrofani R, Santoli C. Posterior pericardial annuloplasty: a physicological correction? *Eur J Cardiothorac Surg.* 1991;5(5):226–229. DOI: 10.1016/1010-7940(91)90168-j
21. Salvador L, Cavarretta E, Minniti G, et al. Autologous pericardium annuloplasty: a "physiological" mitral valve repair. *J Cardiovasc Surg (Torino).* 2014;55(6):831–839.
22. Schroter S, Lamping DL. Coronary revascularisation outcome questionnaire (CROQ): development and validation of a new, patient based measure of outcome in coronary bypass surgery and angioplasty. *Heart.* 2004;90(12):1460–1466. DOI: 10.1136/hrt.2003.021899
23. Scrofani R, Moriggia S, Salati M, et al. Mitral valve remodeling: long-term results with posterior pericardial annuloplasty. *Ann Thorac Surg.* 1996;61(3):895–899. DOI: 10.1016/0003-4975(95)01139-0
24. Sharony R, Saunders PC, Nayar A, et al. Semirigid partial annuloplasty band allows dynamic mitral annular motion and minimizes valvular gradients: an echocardiographic study. *Ann Thorac Surg.* 2004;77(2):518–522. DOI: 10.1016/j.athoracsur.2003.06.005
25. Sidiki AI, Faybushevich AG, Lishchuk AN. A second look at autopericardial mitral annuloplasty. *Cor Vasa.* 2020;62(1):37–43. DOI: 10.33678/cor.2020.003
26. Borghetti V, Campana M, Scotti C, et al. Biological versus prosthetic ring in mitral-valve repair: enhancement of mitral annulus dynamics and left-ventricular function with pericardial annuloplasty at long term. *Eur J Cardiothorac Surg.* 2000;17(4):431–439. DOI: 10.1016/s1010-7940(00)00344-4
27. Zerda DJ, Cohen O, Marelli D, et al. Long-term results of mitral valve repair using autologous pericardium annuloplasty. *J Heart Valve Dis.* 2008;17(1):10–15.

СПИСОК ЛИТЕРАТУРЫ

1. Бокерия Л.А., Машина Т.В., Джанкетова В.С., Голухова Е.З. Ультразвуковая анатомия и чреспищеводная трехмерная эхокардиография в хирургии митрального клапана (обзор литературы) // Креативная кардиология. 2014. Т. 8, № 4. С. 65–75.
2. Патент RU 2740122C1/11.01.2021. Вайкин В.Е., Журко С.А., Пименова П.В. и др. Способ пластики митрального клапана аутоперикардиальной полоской при ишемической митральной недостаточности.
3. Гордеев М.Л., Майстренко А.Д., Сухова И.В. и др. Отдаленные результаты использования безимплантационной аннулопластики митрального клапана у пациентов с митральной недостаточностью ишемического генеза // Патология кровообращения и кардиохирургия. 2015. Т. 19, № 1. С. 36–42. DOI: 10.21688/1681-3472-2015-1-36-42
4. Патент RU 2679870C1/13.02.2019. Лищук А.Н., Колтунов А.Н., Есион Г.А., Карпенко И.Г. Способ пластики приобретенного порока митрального клапана.
5. Патент RU 2707262C1/25.11.2019. Сотников А.В., Мельников В.М., Эльмаджи Р.В. Способ профилактики послеоперационного переднего медиастинита после выполнения полной продольной стернотомии при открытых операциях на сердце.
6. Шнейдер Ю.А., Талипов И.Р., Ужахов И.Р. Изменения внутрисердечной гемодинамики при пластике митрального клапана синтетической полоской // Вестник хирургии имени И.И. Грекова. 2011. Т. 170, № 5. С. 54–56.
7. Alfieri O., Lapenna E. Systolic anterior motion after mitral valve repair: where do we stand in 2015? // Eur. J. Cardiothorac. Surg. 2015. Vol. 48, No. 3. P. 344–346. DOI: 10.1093/ejcts/ezv230
8. Barlow C.W., Ali Z.A., Lim E. et al. Modified technique for mitral repair without ring annuloplasty // Ann. Thorac. Surg. 2003. Vo. 75, No. 1. P. 298–300. DOI: 10.1016/s0003-4975(02)03924-3
9. Brown M.L., Schaff H.V., Li Z. et al. Results of mitral valve annuloplasty with a standard-sized posterior band: is measuring

important? // J. Thorac. Cardiovasc. Surg. 2009. Vol. 138, No. 4. P. 886–891. DOI: 10.1016/j.jtcvs.2009.01.022
10. Bruno V.D., Di Tommaso E., Ascione R. Annuloplasty for mitral valve repair in degenerative disease: to be flexible or to be rigid? That's still the question // Indian J. Thorac. Cardiovasc. Surg. 2020. Vol. 36, No. 6. P. 563–565. DOI: 10.1007/s12055-020-01001-3
11. Cahill T.J., Prothero A., Wilson J. et al. Community prevalence, mechanisms and outcome of mitral or tricuspid regurgitation // Heart. 2021. Vol. 107, No. 12. P. 1003–1009. DOI: 10.1136/heartjnl-2020-318482
12. Calafiore A.M., Di Mauro M., Gallina S. et al. Optimal length of pericardial strip for posterior mitral overreductive annuloplasty // Ann. Thorac. Surg. 2003. Vol. 75, No. 6. P. 1982–1984. DOI: 10.1016/s0003-4975(02)04685-4
13. Gillinov A.M., Cosgrove D.M.3d., Shiota T. et al. Cosgrove-Edwards Annuloplasty System: midterm results // Ann. Thorac. Surg. 2000. Vol. 69, No. 3. P. 717–721. DOI: 10.1016/s0003-4975(99)01543-x
14. Hetzer R., Delmo Walter E.M. No ring at all in mitral valve repair: indications, techniques and long-term outcome // Eur. J. Cardiothorac. Surg. 2014. Vol. 45, No. 2. P. 341–351. DOI: 10.1093/ejcts/ezt322
15. Nishi H., Toda K., Miyagawa S. et al. Annular dynamics after mitral valve repair with different prosthetic rings: A real-time three-dimensional transesophageal echocardiography study // Surg. Today. 2016. Vol. 46, No. 9. P. 1083–1090. DOI: 10.1007/s00595-015-1279-z
16. Omay O., Ozker E., Indelen C. et al. Posterior pericardial annuloplasty in ischemic mitral regurgitation // Heart Surg. Forum. 2009. Vol. 12, No. 5. P. E285–290. DOI: 10.1532/HSF98.20091006
17. Onorati F., Santini F., Dandale R. et al. Functional mitral regurgitation: a 30-year unresolved surgical journey from valve replacement to complex valve repairs // Heart Fail. Rev. 2014. Vol. 19, No. 3. P. 341–358. DOI: 10.1007/s10741-013-9392-9
18. Padang R., Ali Y.Z., Mankad R. et al. Thromboembolic complications of annuloplasty rings // JACC Cardiovasc. Imaging. 2021. Vol. 14, No. 8. P. 1659–1665. DOI: 10.1016/j.jcmg.2020.08.038
19. Roshanali F., Vedadian A., Shoar S. et al. The viable mitral annular dynamics and left ventricular function after mitral valve repair by biological rings // Int. Cardiovasc. Res. J. 2012. Vol. 6, No. 4. P. 118–123.
20. Salati M., Scrofani R., Santoli C. Posterior pericardial annuloplasty: a physicological correction? // Eur. J. Cardiothorac. Surg. 1991. Vol. 5, No. 5. P. 226–229. DOI: 10.1016/1010-7940(91)90168-j
21. Salvador L., Cavarretta E., Minniti G. et al. Autologous pericardium annuloplasty: a "physiological" mitral valve repair // J. Cardiovasc. Surg. (Torino). 2014. Vol. 55, No. 6. P. 831–839.
22. Schroter S., Lamping D.L. Coronary revascularisation outcome questionnaire (CROQ): development and validation of a new, patient based measure of outcome in coronary bypass surgery and angioplasty // Heart. 2004. Vol. 90, No. 12. P. 1460–1466. DOI: 10.1136/hrt.2003.021899
23. Scrofani R., Moriggia S., Salati M. et al. Mitral valve remodeling: long-term results with posterior pericardial annuloplasty // Ann. Thorac. Surg. 1996. Vol. 61, No. 3. P. 895–899. DOI: 10.1016/0003-4975(95)01139-0
24. Sharony R., Saunders P.C., Nayar A. et al. Semirigid partial annuloplasty band allows dynamic mitral annular motion and minimizes valvular gradients: an echocardiographic study // Ann. Thorac. Surg. 2004. Vol. 77, No. 2. P. 518–522. DOI: 10.1016/j.athoracsur.2003.06.005
25. Sidiki A.I., Faybushevich A.G., Lishchuk A.N. A second look at autopericardial mitral annuloplasty // Cor. Vasa. 2020. Vol. 62, No. 1. P. 37–43. DOI: 10.33678/cor.2020.003
26. Borghetti V., Campana M., Scotti C. et al. Biological versus prosthetic ring in mitral-valve repair: enhancement of mitral annulus dynamics and left-ventricular function with pericardial annuloplasty at long term // Eur. J. Cardiothorac. Surg. 2000. Vol. 17, No. 4. P. 431–439. DOI: 10.1016/s1010-7940(00)00344-4
27. Zerda D.J., Cohen O., Marelli D. et al. Long-term results of mitral valve repair using autologous pericardium annuloplasty // J. Heart Valve Dis. 2008. Vol. 17, No. 1. P. 10–15.

AUTHORS INFO

*** Artem V. Sotnikov**, MD;
address: 41 Kirochnaya St., Saint Petersburg, 191015, Russia;
ORCID: https://orcid.org/0000-0003-1831-7025;
e-mail: artem.sotnikov@szgmu.ru

Michail V. Melnikov, MD, Professor;
ORCID: https://orcid.org/0000-0003-2215-3369;
e-mail: memivik@yandex.ru

ОБ АВТОРАХ

*** Артем Владимирович Сотников**;
адрес: Россия, 191015, Санкт-Петербург, Кирочная ул., д. 41;
ORCID: https://orcid.org/0000-0003-1831-7025;
e-mail: artem.sotnikov@szgmu.ru

Михаил Викторович Мельников, профессор;
ORCID: https://orcid.org/0000-0003-2215-3369;
e-mail: memivik@yandex.ru

* Corresponding author / Автор, ответственный за переписку

AUTHORS INFO

Anna M. Bitieva, MD;
ORCID: https://orcid.org/0000-0002-5383-2367;
e-mail: anna.bitieva@szgmu.ru

Eduard A. Kolmakov;
ORCID: https://orcid.org/0000-0002-0553-0081;
e-mail: rectorat@szgmu.ru

ОБ АВТОРАХ

Анна Мурмановна Битиева;
ORCID: https://orcid.org/0000-0002-5383-2367;
e-mail: anna.bitieva@szgmu.ru

Эдуард Александрович Колмаков;
ORCID: https://orcid.org/0000-0002-0553-0081;
e-mail: rectorat@szgmu.ru