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A new method of left atrial appendage occlusion for the prevention of thromboembolic complications in patients with atrial fibrillation during coronary artery bypass grafting

Vechersky Yu. Yu., Bogdanov Yu. I., Batalov R. E., Zatolokin V. V., Saushkin V. V., Zavadovsky K. V., Popov S. V.

Aim. To optimize the surgical technique for left atrial appendage (LAA) occlusion in patients with atrial fibrillation (AF) during coronary artery bypass grafting.

Material and methods. The study included 60 patients with atrial fibrillation (AF). The patients were randomly divided into 2 groups. In the first group of patients, LAA was closed using the developed two-suture technique. In patients of the second group, a purse string suture was applied to the LAA. All patients underwent transesophageal echocardiography (TEE) before surgery to rule out the presence of intracardiac blood clots. To assess the effectiveness of the method in the postoperative period, TEE was performed.

Results. According to postoperative TEE, one case of LAA recanalization in each group was revealed (p>0,05). In the second group, the residual LAA cavity after applying a purse string suture was revealed. During the follow-up period, there were no neurological complications and deaths.

Conclusion. According to the study results, it was found that the proposed two-suture technique for LAA occlusion is not less effective than the purse-string suture. The developed technique of two-suture epicardial occlusion of LAA showed actual technical advantages, allowing to optimize this surgery in different categories of patients.

Key words: atrial fibrillation, left atrial appendage, coronary artery bypass grafting.

Relationships and Activities: none.

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Atrial fibrillation (AF) is the most common type of arrhythmia in clinical practice. AF remains the leading cause of cardioembolic stroke, increasing the risk of cerebrovascular accident 5-fold compared to patients without AF. In patients with nonvalvular AF, the localization of thrombi in the left atrial appendage (LAA) reaches 90% [1, 2]. A variety of surgical approaches have been proposed for LAA occlusion, including suture exclusion, suture excision, stapler exclusion, epicardial exclusion clips. All of these techniques aim to exclude LAA completely to prevent blood clotting. For the first time, the reliability of LAA ligation was evaluated in the early 2000s. After mitral valve surgery and LAA ligation, incomplete exclusion was found in 36% of patients, according to transesophageal echocardiography (TEE) [3]. These results challenged the assumption that surgical exclusion of LAA is always complete and highlighted the need to test the reliability of the intervention.

In the Left Atrial Appendage Occlusion Study (LAAOS), patients after coronary artery bypass grafting were divided into groups of ligation or stapler exclusion of LAA and a control group [4]. Eight weeks after surgery, complete LAA occlusion by ligation was found in only 45% of patients, while stapler exclusion was successful in 72% of patients. Failure to exclude LAA was defined as residual flow into the appendage cavity or a neck >1 cm. The authors concluded that LAA exclusion does not significantly lengthen the cardiopulmonary bypass duration and does not increase the number of postoperative complications, such as bleeding and AF.

Due to the shortcomings of traditional surgical techniques for LAA occlusion, surgical devices have been developed. The effectiveness of these devices primarily depends on their ability to maintain high occlusal pressure. Of the available devices, the AtriClip device has the most clinical experience [5]. Thus, in the EXCLUDE trial, the effectiveness of the AtriClip device was >95% in cardiac surgery patients with a high risk of ischemic stroke [6].

Despite the introduction of highly effective devices for LAA occlusion, the indisputable advantage of suture techniques is the possibility of their use in any shape of LAA, which in some cases is a limitation to the use of occlusion devices.

Material and methods

The prospective study included 60 patients with persistent AF. The patients were divided into 2 groups using the envelope method. The study was approved by the local ethics committee. All patients signed an informed consent. The study included patients with documented AF and indications for myocardial revascularization. The study did not include patients with left ventricular aneurysm, reduced ejection fraction (<40%), and contraindications to anticoagulants. The average age of patients was 62,9±7,1 and 63,7±7,2 in the first and second groups, respectively. In both groups, men predominated (n=53). The patients were comparable in the prevalence of diabetes, history of myocardial infarction, and duration of AF. The baseline characteristics of patients are presented in Table 1. In addition to antiarrhythmic therapy, patients received medical therapy for heart failure, coronary artery disease, and hypertension (Table 2). In the first group of patients, LAA was switched off using the developed two-suture method. In patients of the second group, a purse string suture was applied to the LAA. Patients of the first and second groups underwent epicardial radiofrequency isolation of the pulmonary veins, posterior wall, and LAA using AtriCure electrodes. Initially, bipolar radiofrequency isolation of the right and left pulmonary veins was performed. The right and left pulmonary veins were isolated alternately with a power of 25 W. Then the electrode was passed through the LAA puncture towards the right superior pulmonary vein, thereby creating a line along the left atrial (LA) roof. A line was performed connecting the inferior pulmonary veins. Then the LAA base was ablated.

Table 1

Baseline patient characteristics

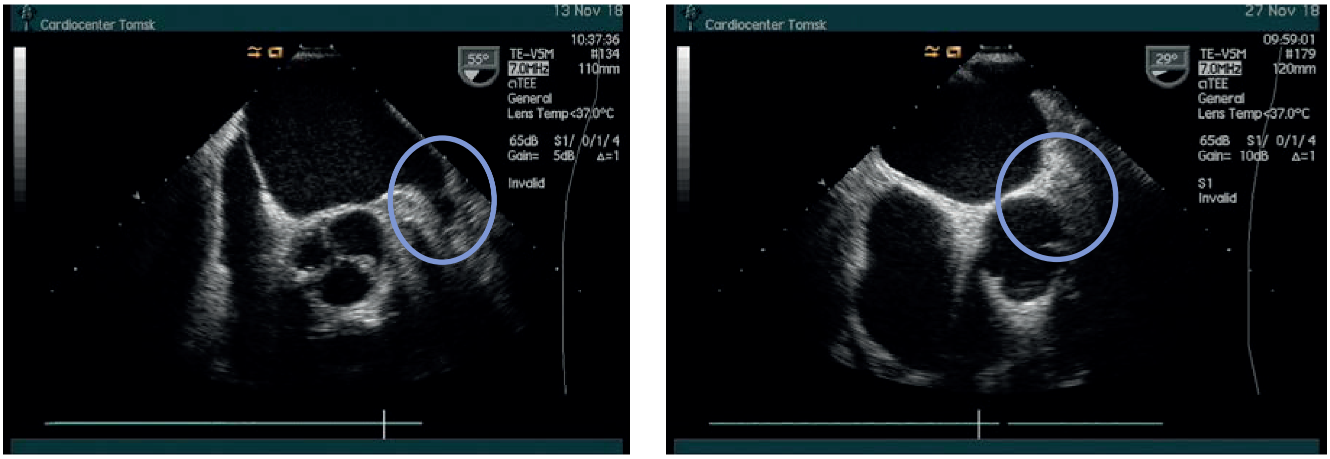
Parameter	Group 1 (n=30)	Group 2 (n=30)	p value
Age (years)	62,9±7,1	63,7±7,2	p>0,05
Men	26 (86,6%)	27 (90%)	p>0,05
Women	4 (13,4%)	3 (10%)	
Previous CVA	1 (3,3%)	1 (3,3%)	p>0,05
CKD	2 (6,6%)	1 (3,3%)	p>0,05
Diabetes	5 (16,6%)	7 (23,3%)	p>0,05
Previous MI	16 (53,3%)	14 (46,6%)	p>0,05

Abbreviations: CVA — cerebrovascular accident, CKD — chronic kidney disease, MI — myocardial infarction.

Table 2

Therapy received by study participants

Medication classes	Number of patients, n (%)	
	Group 1	Group 2
Beta-blockers	19 (63,3%)	25 (83,3%)
Angiotensin-converting enzyme inhibitors	24 (80%)	12 (40%)
Angiotensin II receptor blockers	5 (16,6%)	8 (26,6%)
Diuretics	23 (76,6%)	25 (83,3%)
Statins	30 (100%)	23 (76,6%)
Hypoglycemic agents	5 (16,6%)	7 (23,3%)



A B

Figure 1 (A, B). A: Preoperative TEE, **B**: Postoperative TEE (two-suture technique).

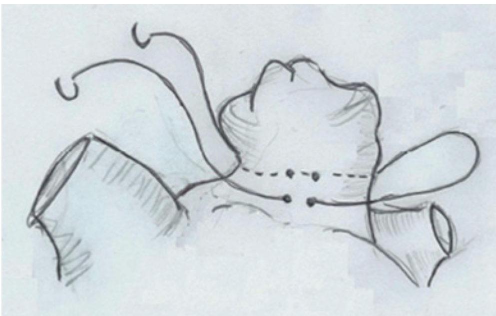


Figure 2. Exclusion of LAA using two-suture technique.

All patients underwent TEE before surgery to rule out the presence of intracardiac blood clots. There were no blood clots in the cardiac cavities before surgery. To evaluate the effectiveness of the method, all patients underwent postoperative TEE (Figure 1). For illustrative purposes, a number of patients underwent multislice computed tomography of the LA. The follow-up period was 12 months.

The novel two-suture LAA occlusion technique was carried out in the following order (Figure 2): after standard sternotomy and pericardiotomy, a standard conduit isolation was performed. Next, a patient was connected to the cardiopulmonary bypass machine. After the distal anastomoses are applied, the LAA is retracted to the side to visualize the inner surface of LAA base. Then one suture is applied on the medial surface in the area of LAA base. Then the LAA is retracted towards the heart and a second suture is applied on the lateral surface at the LAA base. Next, the thread is tied at the LAA base in the area of LA roof.

To assess qualitative differences, the chi-squared test and Fisher's exact test were used. Differences were considered significant at $p<0,05$. All statistical calculations were performed using the Statistica 10.0 software (StatSoft, USA).

Results

According to TEE, recanalization of LAA in the early postoperative period was registered in one patient of each group. In both cases, the shunt volume was insignificant and was considered as hemodynamically insignificant (Table 3). In the

Table 3

Results

	Two-suture technique	Purse-string suture	p
Recanalization of LAA	1 (3,3%)	1 (3,3%)	p>0,05
Residual LAA cavity	0	1 (3,3%)	p>0,05
Neurological complications	0	0	p>0,05

Abbreviation: LAA — left atrial appendage.

patient of the second group, a residual LAA cavity was due to incomplete capture of the LAA base (Figure 3). During the 12-month follow-up period, there were no cases of neurological complications and deaths.

A three-dimensional reconstruction of the LA obtained before the surgery shows LA with a wide base (Figure 4A). The tomogram obtained 10 days after the operation (Figure 4B) demonstrates the constricted base and no contrast in the LAA, which confirms its complete occlusion.

A novel method of LAA occlusion was developed for thromboembolism prevention. The developed method is not inferior in efficiency to standard methods of occlusion, is easily reproducible and complements the radiofrequency electrical isolation of the LAA.

The described method allows minimizing manipulations on the LA, does not require significant dislocation of the heart and provides complete occlusion of LAA at its base without residual volume.

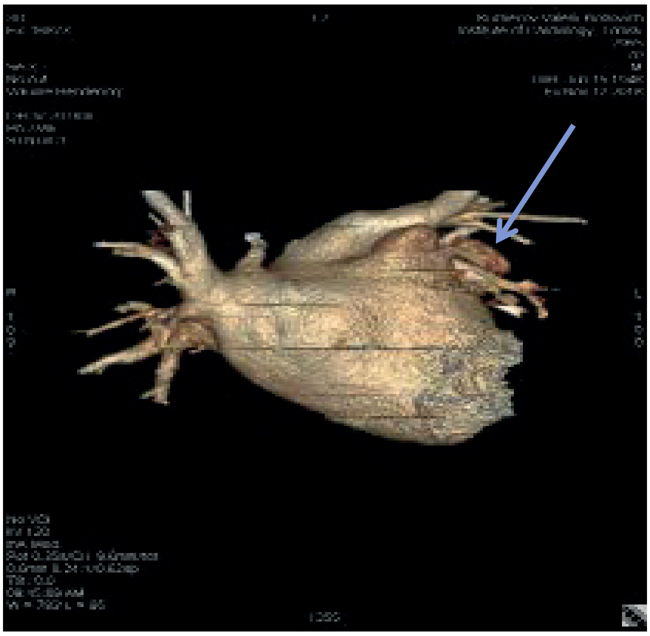


Figure 3. Three-dimensional reconstruction of LA. The arrow indicates the residual LAA cavity after the purse-string suture.

A **B**

Figure 4 (A, B). Three-dimensional reconstruction of LAA. **A** — before exclusion, **B** — after exclusion using two-suture technique.

Discussion

In this study, all patients with AF underwent LAA exclusion during coronary artery bypass grafting, which is consistent with the 2019 guidelines for the management of AF patients, in which the class of recommendation for surgical occlusion of LAA remains IIb, but the level of evidence has increased from C to B [7]. Thus, in the 2019 meta-analysis, which included over 280,000 patients, a protective effect was shown against cerebrovascular accident and thromboembolic events in studies where the proportion of patients with AF was >70% [8]. Mortality in the medium- and long-term period was also significantly lower in patients who underwent surgical occlusion of LAA. Thus, surgical occlusion of LAA, as a concomitant procedure to the main intervention, is associated with a decrease in the risk of strokes and embolic events.

However, despite the available evidence in favor of LAA exclusion, this intervention is not performed in all patients with AF during cardiac surgery. Refusal to occlude LAA is explained by the its fragile anatomical structure, and possible complications are difficult to treat [9].

In our study, recanalization was detected in one patient (3,3%) in the two-suture group and in one patient (3,3%) in the purse-string suture group. In one of the studies, LAA recanalization after its suturing and stapler exclusion was also shown. Only in the case of its resection, no residual flow was observed, but at the same time a residual stump containing thrombotic masses was detected in 25% of cases [10].

Despite the fact that LAA resection is more effective than epicardial occlusion, this method is poorly accepted in minimally invasive surgery due to its complexity [10]. Resection of LAA requires more time, is quite injurious and is associated with bleeding risk, and in addition, there may be non-resected areas of LAA [11]. Thus, it was necessary to improve the suture technique. The technology of two-suture epicardial occlusion of LAA was developed, which combines the reliable fixation of the purse-string technique and the availability of ligation. It is easily reproducible, does not require special skills and tools, significantly reduces the number of manipulations, takes into account the geometry of LAA, and can be performed in minimally invasive approaches. In this study, the efficacy and safety of this method was to be examined. The study showed that the novel method is not inferior to the purse-string suture in the efficiency of LAA exclusion, but at the same time, in contrast to the purse, it is simpler, faster and more promising with limited approach. The technical advantage of this method is the ability to exclude the LAA with one thread using two sutures, minimizing its mechanical damage.

It should be emphasized that the most reliable way to prevent thromboembolic complications is to achieve and maintain sinus rhythm. LAA exclusion, along with radiofrequency fragmentation of the LA, makes an additional contribution to LA electrical isolation and thereby contributes to the maintenance of sinus rhythm.

Study limitations. Since all participants had documented AF, each patient received anticoagulants in the pre- and postoperative period. In the present study, it is difficult to assess the true efficacy of LAA exclusion in the prevention of thromboembolic complications while taking anticoagulants. Further research is needed to study the associations and role of LAA occlusion in patients without documented AF.

Conclusion

Thus, the proposed method of LAA exclusion by a two-suture technique is an effective and safe way to prevent thromboembolism in patients with AF after CABG. The presented method of two-suture exclusion of LAA is not inferior to the standard purse-string suture in preventing strokes, while being simpler and faster to apply.

Relationships and Activities: none.

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Experience of heart transplantation with an extended cold ischemic time of donor heart

Fomichev A. V., Khvan D. S., Agaeva H. A., Zhulkov M. O., Doronin D. V., Chernyavsky A. M.

Aim. A retrospective analysis of the outcomes of heart transplantation (HT) with extended cold ischemic time of donor heart (more than 4 hours) versus heart transplantation with short cold ischemia time (less than 4 hours).

Material and methods. The retrospective analysis included 52 recipients who underwent HT in the period from July 20, 2012 to October 23, 2019 in Meshalkin National Medical Research Center. The patients were divided into two groups: group 1 (n=26) — orthotopic HT with extended cold ischemic time (more than 240 minutes), group 2 (n=26) — short cold ischemia time (less than 240 minutes). The effect of cold ischemia duration on hospital survival, the function of donor heart, and the postoperative course was assessed.

Results. A retrospective analysis revealed a higher rate of hospital survival in the group of recipients with extended cold ischemic time (more than 240 minutes) — 88,5% compared to 80,7% in the second group. There was no difference between the groups in the acute rejection rate, the need for inotropic agents, mechanical circulatory support, and cardiac pacing, as well as the incidence of postoperative renal failure and infectious complications.

Conclusion. Due to the small number of patients, our experience in HT with extended cold ischemic time does not allow us to draw global conclusions, but a preliminary comparison of HT with extended and short cold ischemic time did not reveal significant advantages in one group or another. This provides a basis for further accumulation of experience and research.

Key words: heart transplantation, cold ischemia, heart failure.

Relationships and Activities: none.

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End-stage heart failure (HF) remains a major healthcare problem. Heart transplantation (HT) is a key treatment for end-stage HF. The problem of a critical donor organ shortage and an increase in the need for HT specify the expansion of criteria for selecting donors — age, function, ischemic time of donor heart.

Currently, the recommended cold ischemia time (CIT) is <4 hours, and an increase in the heart preservation duration is associated with an increased risk of ischemia-reperfusion injury, graft dysfunction, and mortality [1].

Already in 1995, analysis of CIT effect on the short- and long-term results of orthotopic HT (oHT). It was revealed that CIT was not a predictor of graft dysfunction and did not affect short- and long-term survival [2].

US authors presented more contradictory data, where the donor older age, regardless of the CIT, was a predictor of mortality. And an increase in the CIT to 6 hours is the best option for critical recipients [3].

Despite many studies, the question of the safe CIT remains open; there is no clear limit for preservation time. At the same time, it is complicated by various methods of donor heart preservation, small numbers of studies, and the heterogeneous structure of recipients.

Which recipients need oHT with prolonged CIT? Which preservative solution is best used in this case? Are there any postoperative features? There are no definite answers to these questions yet.

There are data showing that a young donor organ tolerates prolonged ischemia better than an older one. A shorter CIT improves survival in elderly HT recipients [4, 5]. Obviously, a donor age and the estimated ischemia time should be taken into account to improve the survival of HT recipients [4-6].

Undoubtedly, promising areas are the development of more effective methods for donor organ preservation and normothermic perfusion.

At the same time, it is necessary to minimize extra- and intracellular edema, intracellular acidosis, and to reduce the free radical formation. There are many studies aimed at optimizing preservation methods in order to increase the safe CIT and to reduce myocardial damage associated with prolonged ischemia [7].

The article presents the experience of oHT with prolonged ischemia time at the E. N. Meshalkin National Medical Research Center.

Material and methods

The retrospective analysis included 52 recipients: 43 men and 9 women who underwent oHT in the period from July 20, 2012 to October 23, 2019. The patients were divided into two groups depending on the CIT. The first group of the study included 26 recipients who underwent oHT with prolonged CIT of heart (>240 min); the second group — 26 recipients with short CIT (<240 min). The baseline characteristics of the recipients are presented in Table 1. In all cases, prolonged ischemia was due to long-term transportation from remote regions: Krasnoyarsk Krai, Kemerovo Oblast, Altai Krai.

All organ harvesting was performed from brain-dead donors. The age of the donors ranged from 23 to 56 years. The median age in the prolonged CIT group was 40 (34-46) years, in the short CIT group — 43 (40-51) years. The selection criteria were standard, donors with expanded criteria were not considered. Surgical and heart preservation techniques were standard.

All patients underwent oHT using the standard bicaval technique.

All patients underwent control transthoracic echocardiography immediately after surgery, on days 5-10, and after 1 month. The function and volumetric characteristics of the recipient's heart chambers after transplantation and the pulmonary artery pressure were assessed. Based on the results of a histological study of an endomyocardial biopsy, the level of rejection was assessed according to the ISHLT-WF classification (International Society for Heart and Lung Transplantation — working formulation, 2004).

In-hospital survival was considered as the primary endpoint. Secondary endpoints included the inotropic score at the time of disconnection from the heart-lung bypass machine, differences in the graft dysfunction incidence and the need for perioperative mechanical circulatory support, graft rejection, and analysis of risk factors for postoperative complications.

Given the small sample size and non-normal distribution (according to the Shapiro-Wilk test), the data are presented as median and first and third quartiles. We used the Mann-Whitney test for comparison of independent samples. Univariate regression was used to identify predictors of mortality.

Results

In-hospital survival in the prolonged CIT group was 88,5% (n=23), where 3 deaths were recorded (11,5%). At the same time, all three deaths in group 1 was due to graft dysfunction in the early postoperative period. All three patients belonged to the urgency status 2 in accordance with the United Network of Organ Sharing guidelines (1989). In one case, the cause was severe right ventricular failure after disconnection of extracorporeal membrane oxygenation (ECMO), in another case — large intraoperative bleeding in the patient with coagulopathy and severe decompensated heart failure, which was due to the extremely severe pre-transplantation sta-

Table 1

Baseline characteristics of recipients

Parameter	Group 1 (>240 min)	Group 2 (⩽240 min)
Age, years	41,5 [32,25-48,75] (21-66)	47 [33,75-50] (13-61)
BMI, kg/m^2	25,15 [21,65-27,45]	25 [23,5-31,975]
Sex		
Men Women	19 (73%) 7 (27%)	24 (92%) 2 (8%)
Primary diagnosis		
DCM	19 (73%)	13 (50%)
ICM	5 (19,2%)	10 (38,4%)
HCM	0	1 (3,8%)
Rheumatism	0	1 (3,8%)
Myocarditis	0	1 (3,8%)
Tumor	1 (3,8%)	
Congenital heart disease	1 (3,8%)	
Cold ischemia time of allograft, min	349,5 [300-397,5] (240-456)	173,5 [155,75-185,25] (135-240)
UNOS status 1a 1b 2	 4 (15,4%) 5 (19,2%) 17 (65,4%)	 2 (7,7%) 1 (3,8%) 23 (88,5%)

Abbreviations: HCM — hypertrophic cardiomyopathy, DCM — dilated cardiomyopathy, ICM — ischemic cardiomyopathy, BMI — body mass index.

tus of the recipient. OHT for this patient was a desperate operation.

In-hospital survival in the second group (<240 min) was 80,8% (n=21), where 5 deaths were recorded (19,2%), respectively. There were following causes of deaths: multiple organ failure (n=1), sepsis (n=1), acute rejection (n=1), and graft dysfunction (n=2).

According to the Kaplan-Meier survival estimates, there was no difference between the groups (log-rank, P 1/4 0,8025) (Figure 1).

Thus, primary graft dysfunction in the early postoperative period was observed in 11,5% (n=3) in the first group, and in 19,2% (n=5) in the second group.

Mechanical circulatory support (MCS) as a bridge to transplantation was performed in 8 patients (30,7%) from group 1 and 3 patients from group 2 (11,5%).

ECMO as a bridge to oHT in the first group was performed in one patient (3,8%). Due to hemodynamic instability and high-dose inotropic support, it was decided to reconnect ECMO immediately after surgery. MCS in the early postoperative period in the prolonged CIT group was needed only by 4 patients (15,4%), in the group with short CIT — by 3 patients (11,5%).

The level of inotropic support at the time of disconnection from cardiopulmonary bypass machine is represented by the inotropic score, while no

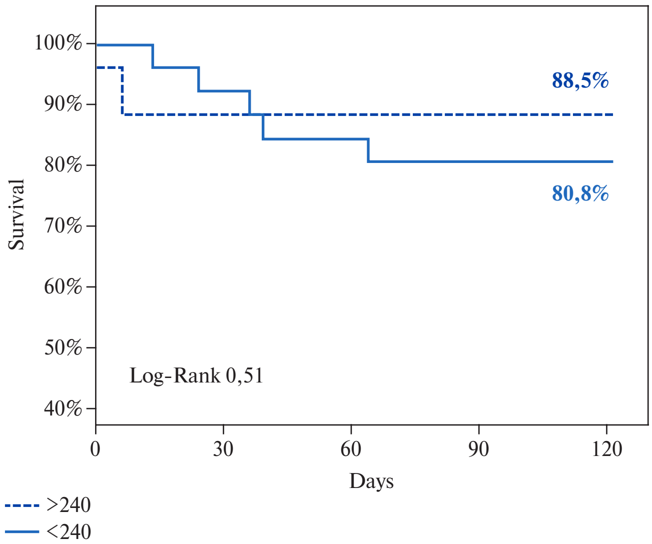

Figure 1. Kaplan-Mayer survival analysis in groups.

significant difference was found between the two groups (p=0,13). The median inotropic score in the 1st group was 8 (4-14,75), in the 2nd — 6,75 (325-8).

Univariate analysis revealed that significant predictors of in-hospital mortality were a decrease in heart graft contractility (hazard ratio, 10,97; 95% confidence interval, 2,64-54,24; p=0,0014), while

Table 2

Endomyocardial biopsy results

Results of endomyocardial biopsy according to ISHLT-WF (1990) criteria	No rejection	1A и 1B	2 и 3A	3B и 4
Perioperative period				
Group with ischemia >240 min	57,6% (n=15)	38,4% (n=10)		3,8% (n=1)
Group with ischemia ⩽240 min	73,1% (n=19)	19,2% (n=5)	3,8% (n=1)	3,8% (n=1)
One month after surgery				
Group with ischemia >240 min	61,5% (n=16)	30,7% (n=8)	7,7% (n=2)	
Group with ischemia ⩽240 min	84,6% (n=22)	11,5% (n=3)	3,8% (n=1)	

Table 3

Transthoracic echocardiography dynamics in recipients after HT

	Group with ischemia ⩽240 min	Group with ischemia >240 min	p
Indicators for 5-10 days after surgery			
LV EDV, ml	70,6 [60,25-76,25]	70 [49-90]	p=0,94
LV ESV, ml	29 [19,875-31]	15,5 [12,75-31,15]	
RV EDV, ml	35,5 [28,675-44,5]	33,5 [28,125-43,75]	
LVEF, %	60,5 [56,25-64,75]	61 [55-66]	p=0,66
RV FAC, %	41,5 [38,5-51,5]	41 [38-43]	
IVS thickness, mm	12,5 [11-14]	14 [13-16]	
LVPW thickness, mm	12 [10,25-14,5]	13 [12-15]	
Pulmonary artery pressure (mm Hg)	30 [27,5-32,75]	32 [28,5-36,5]	
Indicators 1 month after surgery			
LV EDV, ml	71 [66-74]	86 [61-90]	p=0,47
LV ESV, ml	21 [19,9-30]	29 [20,75-32,75]	
RV EDV, ml	34 [32-41,5]	36,5 [32-46]	
LVEF, %	65 [61-66]	65 [59,25-70]	p=0,86
RV FAC, %	46 [45-48]	45 [40-46]	
IVS thickness, mm	14 [12-15]	13 [13-15,75]	
LVPW thickness, mm	12,5 [12-13,5]	14 [12-15]	
Pulmonary artery pressure (mm Hg)	30 [28-33]	31 [30-33,5]	

Abbreviations: LVPW — left ventricular posterior wall, LV EDV — left ventricular end-diastolic volume, LV ESV — left ventricular end-systolic volume, RV EDV — right ventricular end-diastolic volume, IVS — interventricular septum, LVEF — left ventricular ejection fraction, RV FAC — right ventricular fractional area change.

ischemia time and mechanical support before oHT did not affect mortality.

The need for renal replacement therapy after oHT was the same in both groups — 3,8% (n=1).

There were no differences in the rates of MCS, postoperative renal failure, the need for cardiac pacing, and infectious complications.

There were no significant differences in the groups in the frequency of in-hospital acute cellular rejection. In group 1, there was 1 case of severe rejection and 2 cases of moderate rejection. In the 2nd group, there was one case of severe and moderate rejection. Endomyocardial biopsy results are shown in Table 2.

Cardiac pacing was required in two cases (7,6%) in the group of prolonged CIT and in three cases (11,5%) in the short ischemia group.

All patients underwent transthoracic echocardiography. The volumetric characteristics and mechanical activity of the recipient's heart chambers after transplantation were evaluated. The results of postoperative echocardiography are presented in Table 3.

The assessment of left ventricular (LV) end-diastolic volume and LV ejection fraction did not reveal significant difference between the groups. At the same time, there was a significant difference within the group in LV ejection fraction (p=0,03 and p=0,02, in the 1st and 2nd groups, respectively), but there were no differences in LV end-diastolic volume (p=0,31, p=0,54, in the 1st and 2nd groups, respectively).

Discussion

HT is a key treatment for end-stage HF. The problem of a critical donor organ shortage and an increase in the need for HT specify the introduction of expanded criteria donors and donor hearts with prolonged CIT. Currently, the recommended cold ischemia time (CIT) is <4 hours. In a situation where the estimated CIT may exceed 4 hours, it is necessary to use hearts from young donors with normal function and little inotropic support [1].

According to this comparative analysis, we did not find a significant difference in in-hospital survival in the study groups. Undoubtedly, based on these data alone, we cannot recommend increasing the allowable ischemic time. A much larger-scale analysis of the effect of donor heart CIT on recipient survival after oHT is required.

According to many studies, the short- and long-term results of oHT with short- and long-term ischemia are comparable [8-11], which is consistent with our data. Univariate regression did not reveal the effect of CIT on in-hospital survival.

Shafiq F, et al. from Wuhan Union Hospital in China presented the experience of 297 HTs, evaluating the effect of CIT (>8, 6-8, 4-6 and <4 hours) on survival rates. In their opinion, donor hearts with CIT <8 h can be safely used to increase the donor pool. CIT >8 h was a predictor of a higher mortality rate compared with the other three groups during the 2-year follow-up, as well as longer cardiopulmonary bypass [10].

The interesting analysis was presented by Gaffey AC, et al. [12]. Authors analyzed the results of 25,996 oHTs conducted for the period from January 2000 to December 2013. The effect of the distance from the donor to the transplant center and the CIT on 1- and 5-year survival was evaluated. It was concluded that with the correct selection of the donor-recipient pair, the distance and CIT of the cardiac allograft does not affect 1- and 5-year survival. Also, there was no difference in the risk of stroke, the need for dialysis and reoperations in the groups [12].

The retrospective cohort study by British Columbia researchers revealed that an increase in cardiac allograft ischemia time was not associated with a significant difference in 10-year survival.

In another analysis, the total ischemic time of the cardiac allograft also did not affect survival. However, the effect of prolonged CIT on survival has been proven if the donor's age was >50 years (p=0,009) [9].

In our opinion, the interest in the prolonged CIT of cardiac allograft by foreign authors has somewhat decreased. This is due to the fact that the central ways to solve the problem of donor shortages in developed countries is the development of perfusion technologies. Promising results are demonstrated by the Transmedics organ care system (Transmedics, Inc., USA) and the LifeCradle system (Organ Transport Systems, Inc., USA) [13].

Unfortunately, the use of the above systems of normothermic perfusion in Russia is impossible due to high cost. Currently, the use of heart transplants with cold ischemia for 4-8 h may be one of the main ways to expand the donor pool and increase the availability of HT.

This suggests itself that it is necessary not only to expand the donation criteria and increase the CIT, but also optimize the technology of donor organ preservation, introducing normothermic perfusion systems, and develop methods against ischemia-reperfusion injury.

Conclusion

The short-term outcomes in recipients after HT with prolonged and short ischemia of the cardiac allograft are comparable. The use of donor hearts with long-term ischemia increases the number of HT and reducing the mortality of potential recipients included in the waiting list. According to current study, in-hospital mortality is specified by the severity of the recipient's preoperative condition. It is planned to further accumulate experience on safe CIT of cardiac allograft.

Relationships and Activities: none.

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Features and hospital outcomes of coronary artery bypass grafting in patients with calcification of target coronary arteries

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Aim. To compare strategy and early results of coronary artery bypass grafting (CABG) in patients with and without calcification of target coronary arteries (TCA).

Material and methods. The prospective study analyzed the data of patients (n=462) who underwent elective isolated CABG in 2017-2018 using cardiopulmonary bypass and microsurgery. Two groups were distinguished: group 1 — patients with TCA calcification (n=108), group 2 — patients without TCA calcification (n=354). In cases where the distal coronary artery lesion did not allow standard bypass grafting, additional complex anastomoses were provided. A comparison of intraoperative parameters and early results of CABG was carried out.

Results. In groups 1 and 2, the revascularization index did not differ significantly and was 4,5 and 4,3, respectively. The frequency of complex surgical interventions in group 1 was higher: for example, 'Y' grafts were used in groups 1 and 2, respectively, in 32% (35/108) and 12% (44/354), $p<0,05$; sequential anastomoses — in 14% (15/108) and 7% (26/354), $p<0,05$; prolonged patch-angioplasty — in 21% (23/108) and 5% (16/354), $p<0,05$; anastomoses with arteries <1,5 mm in diameter — in 33% (36/108) and 4% (14/354), $p<0,05$; coronary endarterectomy — in 17% (18/108) and 5% (16/354), $p<0.05$, respectively. The duration of cardio-pulmonary bypass was longer in group 1. At the same time, the hospital clinical results did not differ significantly: mortality was not registered; the frequency of perioperative myocardial infarction was 1,8% (group 1) and 1,1% (group 2); the need for inotropes, frequency of arrhythmia, length of stay in the intensive care unit and hospital were similar; there were no cases of in-hospital angina recurrence.

Conclusion. CABG in patients with calcification of TCA is associated with surgical challenges and need for complex adjunct techniques. Nevertheless, complete surgical revascularization is real in these cases, and the hospital results are comparable to those in patients without calcification.

Key words: coronary artery calcinosis, coronary artery disease, coronary artery bypass grafting.

Relationships and Activities. The study was performed within the research work № 81 under the State Assignment № AAAA-A18-118022290040-7.

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The widespread introduction of endovascular surgery and modern drug treatment of coronary artery disease (CAD) into clinical practice has led to the fact that in recent years, surgeons increasingly operate on elderly patients with severe coronary artery (CA) lesion, history of stenting (including repeated) and many comorbidities. Hypertension, obesity, dyslipidemia, hyperglycemia, familial predisposition, chronic kidney disease, high levels of fibrinogen and C-reactive protein increases the risk of CA calcification (CAC) [1]. According to the study by Wang F, et al. (2018), CAC is observed in more than 90% of men and in more than 67% of women aged over 70 years [2].

CAC in patients with CAD is associated with complications and unsatisfactory clinical outcomes of percutaneous coronary intervention, even when using new-generation stents [3]. Coronary artery bypass grafting (CABG) is equally effective in patients with simple or complex lesions, bypassing which a new vessel is created. However, in published studies, the authors define severe calcification as an independent predictor of worse outcomes after surgery. Ertelt K, et al. (2013) published a study with a 1-year follow-up period and 755 patients after CABG due to acute coronary syndrome, who were included in the Acute Catheterization and Urgent Intervention Triage Strategy (ACUITY) trial. The authors noted that the mortality rates and the incidence of perioperative myocardial infarction (MI) after CABG in patients with CAC were almost 3 times higher than in those without CAC: the one-year mortality rate was 11,8% vs 4,5% (p=0,006), and the prevalence of MI — 31,1% vs 16,4% (p=0,006) [4]. This mortality rate significantly exceeds the general-group level published in the results of modern randomized trials: 3,5% — Surruys PW, et al., SYNTAX trial (2009); 4,2% — Farkouh ME, et al., FREEDOM trial (2012) [5, 6]. Similar results were reported in the study by Bourantas CV, et al. (2015), where patients with severe CAC included in the SYNTAX trial and the SYNTAX CABG registry had a higher 5-year mortality: 17,1% vs 9,9% in the general group (p<0,001), however, differences in the incidence of adverse nonfatal cardiovascular events did not reach significance (26,8% vs 21,8%, p=0,057) [7]. It should be noted that a higher mortality rate, as well as the development of events in groups with CAC, can be interpreted as a result of a more severe comorbidity status (renal failure, hypertension) and multifocal atherosclerosis. Severe CAC was recognized as a significant factor in the increase in mortality and the incidence of cardiovascular events after CABG [4]. The authors note that severe CAC causes technical difficulties in performing distal anastomoses, increases the surgery time length, can lead to vessel wall dissection, distal embolism, and the impossibility of revascularization without endarterectomy; all of these factors may contribute to unsatisfactory outcomes [8].

There are following limitations of the above studies: characterization of calcification was carried out using angiography without the use of highly sensitive methods, such as multislice computed tomography (MSCT) of CA, intravascular ultrasound and optical coherence tomography; the authors did not mention the achievement of complete revascularization; there was no information on the choice of the optimal surgical strategy for the CAC lesions.

The aim was to study the prognostic value of calcification of target coronary arteries (CA) based on the early CABG outcomes in relatively homogeneous groups of patients with complete myocardial revascularization.

Material and methods

The prospective comparative study included 462 patients who underwent elective isolated CABG in the period 2017-2018 at the National Medical Research Center of Cardiology (Russia). Two groups were distinguished: group 1 — patients with TCA calcification (n=108), group 2 — patients without TCA calcification (n=354). The analysis of angiographic data to determine the calcification severity (as well as the assessment of coronary system using the SYNTAX score) was carried out by three independent experts. The target artery was considered calcified if X-ray-positive formations (calcifications) at the level of significant stenoses (occlusions) and distally in the vessel planned for grafting were determined by non-contrast fluoroscopy. In doubtful cases and/or when there was a difference of opinion among experts (in 48 patients), MSCT was performed. In this subgroup, a comparison was made of the diagnostic value of coronary angiography and contrast-enhanced MSCT using a segment involvement score [9]. To assess the coronary bed by segments, the 16-segment American Heart Association classification was used [10]. When the distal diameter was less than the MSCT resolution (<1,5 mm), a vessel- and lesion-specific CAC score was used [11]. Patients with calcification, but without significant coronary artery stenosis, were assigned to group 2.

To reduce the influence of technical factors, CABG was performed in all patients in a standard manner using a cardiopulmonary bypass, cold cardioplegia, and microsurgery. In the vast majority of patients, the left internal thoracic artery was used for myocardial revascularization. In all cases, the tactics of complete revascularization according to the

Table 1

Characteristics of patients

Parameter	Group 1 (n=108)	Group 2 (n=354)	p
Men (%)	79 (73,1%)	270 (76,3%)	NS
Body mass index (M±SD)	28,1±3,5	28±4,2	NS
Age (M±SD)	63,4±7,9	64,5±8,5	NS
Class II angina, n (%) Class III angina, n (%) Class IV angina, n (%)	11 (10,2%) 69 (63,9%) 16 (14,8%)	26 (7,3%) 245 (69,3%) 47 (13,2%)	NS
Unstable angina, n (%)	7 (6,5%)	16 (4,5%)	NS
Silent myocardial ischemia, n (%)	5 (4,6%)	20 (5,7%)	NS
Previous myocardial infarction, n (%)	53 (49,1%)	185 (52,2%)	NS
Ejection fraction, % (M±SD)	57,7±5,3	58,2±7,2	NS
Clinical signs of class >2 HF, n (%)	22 (24,7%)	42 (16,3%)	NS
History of smoking, n (%)	41 (37,9%)	142 (40,1%)	NS
Hypertension, n (%)	92 (85,2%)	268 (75,7%)	NS
Multifocal atherosclerosis, n (%)	47 (43,5%)	92 (25,9%)	<0,05
Diabetes, n (%)	34 (31,5%)	77 (21,7%)	<0,05
CKD ⩽3A, n (%)	6 (5,5%)	10 (2,8%)	NS
Previous CVA, n (%)	11 (10,2%)	9 (2,5%)	<0,05
STS score (M±SD)	0,8±0,4	0,7±0,3	NS

Abbreviations: NS — not significant, HF — heart failure, CVA — cerebrovascular accident, CKD — chronic kidney disease.

Table 2

Preoperative angiographic data

Parameter	Group 1 (n=108)	Group 2 (n=354)	p
Three-vessel lesion, n (%)	106 (98,1%)	345 (97,5%)	NS
LCA trunk lesion, n (%)	17 (15,7%)	51 (14,4%)	NS
SYNTAX score (M±SD)	36±3,7	32±3,6	NS
Previous PCI	23 (21,3%)	73 (20,6%)	NS

Abbreviations: NS — not significant, LCA — left coronary artery, PCI — percutaneous coronary intervention.

SYNTAX trial criteria were used, as well as the principle of revascularization of all three main coronary arteries in three-vessel disease [12]. All patients, starting from the first day after surgery, received antiplatelet therapy with acetylsalicylic acid at a dosage of 100 mg. In the case of coronary endarterectomy, anticoagulant therapy was carried out with infusion of unfractionated heparin starting 6-12 hours after surgery and reaching the target values of activated clotting time (150-170 sec), followed by switching to warfarin with the achievement of an international normalized ratio of 2,0-3,0 with a duration of at least 6 months. All patients, without exception, were prescribed statin therapy: most often, atorvastatin 20-80 mg/day and rosuvastatin 10-20 mg/day.

There were following exclusion criteria: a) significantly reduced contractility of the left ventricle (LV) (LV ejection fraction <35%), b) valvular heart disease requiring surgery, c) LV aneurysm, d) previous MI <1,5 months, e) previous heart surgery.

Early outcomes of CABG were evaluated performing the assessment and comparison of intraoperative data, the need for inotropic support and its duration, the incidence of perioperative MI (PMI), mortality, as well as parameters characterizing postoperative recovery. PMI was diagnosed according to the criteria described Fourth Universal Definition of Myocardial Infarction Guidelines [13].

This study was performed in accordance with the Helsinki declaration and Good Clinical Practice standards. The medical ethics committee approved this study. All patients signed informed consent.

Statistical processing was performed using the Statistica 10.0 software. With a normal distribution, the variables are presented as mean (M) and standard

Table 3

Intraoperative characteristics

Parameter	Group 1 (n=108)	Group 2 (n=354)	p
Mean revascularization index (M±SD)	4,5±0,8	4,3±0,5	NS
Operating microscope use, n (%)	108 (100%)	354 (100%)	NS
Use of LITA, n (%)	104 (96,3%)	351 (99,1%)	NS
Use of PITA, n (%)	7 (6,5%)	38 (10,7%)	NS
Anastomoses with coronary arteries <1,5 mm in diameter, n (%)	36 (33,3%)	14 (4%)	<0,05
Coronary artery endarterectomy, n (%)	14 (12,9%)	17 (4,8%)	<0,05
Prolonged patch-angioplasty, n (%)	23 (21,3%)	16 (4,5%)	<0,05
Sequential anastomoses, n (%)	15 (13,9%)	26 (7,3%)	<0,05
'Y' grafts, n (%)	35 (32,4%)	44 (12,4%)	<0,05
Myocardial ischemia, min (M±SD)	72±18	59±19	<0,05
CPB duration, min (M±SD)	103±24	90±27	<0,05

Abbreviations: NS — not significant, CPB — Cardiopulmonary bypass, LITA — left internal thoracic artery, RITA — right internal thoracic artery.

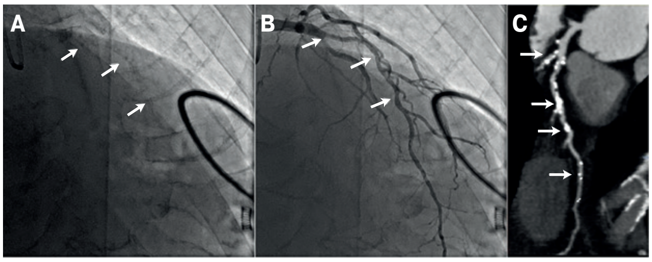

Figure 1 (A, B, C). A. Coronary angiography before contrast enhancement. Arrows indicate calcification in the proximal and middle areas of anterior descending artery (ADA). **B**. Contrast-enhanced coronary angiography. Arrows indicate stenosis in the proximal area and uneven contours in the middle area of ADA. **C**. Multiplanar reconstruction with ADA MSCT. Arrows indicate calcification in the proximal area, pronounced calcification in the middle area, and single calcifications in the distal area of ADA.

deviation (SD). For clinically significant effects, the relative risk and 95% confidence interval (CI) was calculated. To compare two independent groups, the nonparametric Mann-Whitney test was used; to compare the proportions — the chi-squared test or Fisher's exact test. Differences were considered significant at p<0,05.

Results

The mean age of patients in groups 1 and 2 did not differ significantly and amounted to 63,4±7,9 and 64,5±8,5 years, respectively; the vast majority of patients in both groups were men. There were no significant differences between groups for most of the baseline clinical characteristics. However, among patients with calcification, multifocal atherosclerosis, diabetes, and previous cerebrovascular accidents were significantly more frequent. However, the STS score for the risk of surgery were similar in the groups. The demographic and clinical and functional characteristics of the subjects are presented in Table 1.

According to the preoperative coronary angiography (Table 2), multiple CA lesions were noted in all cases. The proportion of patients with left coronary artery stenosis and the SYNTAX score did not differ in the groups. It should be noted that >20% of patients in each group are patients with recurrent angina after percutaneous coronary intervention.

Analysis of the calcification localization showed that, in most cases, calcified lesions were in the three main CAs. The total number of calcified target vessels in 108 patients was 248; in 58 cases, a three-vessel distal lesion was noted. Single vessel calcification was observed in 26 patients; in most cases (n=20), anterior descending artery was involved.

Comparison of diagnostic value of coronary angiography and MSCT in a group of 48 patients who underwent both studies showed that the mean number of detected calcification segments with MSCT is significantly higher than with coronary angiography (8,02±2,6 and 6,02±2, 3, respectively, p<0,05). Figure 1 shows a comparison of images obtained with coronary angiography and MSCT, demonstrating the higher effectiveness of MSCT in detecting distal calcifications.

The frequency of complex surgical interventions in group 1 was higher: 'Y' grafts were used in groups 1 and 2, respectively (odds ratio (OR) 3,4; 95% CI 2,0-5,7; p=0,00005); sequential anastomoses — in 14% (15/108) and 7% (26/354) (OR 2,0; 95% CI 1,0-4,0; p=0,03); prolonged patch-angioplasty — in 21% (23/108) and 5% (16/354) (OR 5,7; 95% CI 2,9-11,3; p=0,0005); anastomoses with arteries <1,5 mm in

Table 4

In-hospital outcomes

Parameter	Group 1 (n=108)	Group 2 (n=354)	p
Bleeding (resternotomy), n (%)	4 (3,7%)	14 (3,9%)	NS
Prolonged mechanical ventilation (>24 h), n (%)	2 (1,8%)	5 (1,4%)	NS
Mean length of stay in ICU, days (M±SD)	2,25±0,8	2,1±0,7	NS
Long-term inotropic support (>24 h), n (%)	4 (3,7%)	10 (2,8%)	NS
Perioperative myocardial infarction, n (%)	2 (1,8%)	4 (1,1%)	NS
Transient encephalopathy, n (%)	10 (9,2%)	31 (8,7%)	NS
Cerebrovascular accident, n (%)	2 (1,8%)	3 (0,8)	NS
Heart rhythm disturbances, n (%)	23 (21,3%)	74 (20,9%)	NS
Postoperative length of stay, days (M±SD)	9,7±3,6	8,8±2,4	NS
Hospital mortality, n (%)	0	0	NS

Abbreviations: NS — not significant, ICU — intensive care unit.

diameter — in 33% (36/108) and 4% (14/354) (OR 12,4; 95% CI 6,2-23,7; p=0,00005); coronary endarterectomy — in 17% (18/108) and 5% (16/354) (OR 2,9; 95% CI 1,4-6,2; p=0,003), respectively. As a result, CABG in both groups had an equivalent and sufficiently high revascularization index. The use of complex surgical interventions in group 1 resulted in an increase in cardio-pulmonary bypass duration (103±24 min vs 90±27 min, p<0,05) and myocardial ischemia (72±18 min vs 59±19 min, p<0,05). Despite this, in-hospital outcomes did not show significant intergroup differences. Intraoperative indicators and in-hospital outcomes of the studied groups are presented in Tables 3 and 4. In the postoperative period, all patients received antiplatelet therapy (aspirin), and in the case of endarterectomy — additionally warfarin; all participants also received statins in a dose depending on lipid levels. Adherence to statin (88,9% vs 90,2%, p>0,05) and antiplatelet therapy (95,1% vs 91,7%, p>0,05) did not differ significantly in both groups.

Discussion

In this work, the distal CAC is considered as a problem that requires an individual approach to the diagnosis and determination of surgical tactics. With the specialized techniques for distal anastomoses, we achieved complete revascularization and favorable in-hospital outcomes. The early outcomes of surgery in patients with/without CCA were similar: hospital mortality was not registered; the incidence of bleeding and resternotomy was comparable; the incidence of perioperative MI was similar. All patients who underwent non-fatal perioperative MI were clinically stable by the end of hospitalization. The need for long-term (>24 h) inotropic support, as well as prolonged (>24 h) mechanical ventilation in the groups was similar. The frequency of arrhythmia, length of stay in the intensive care unit and hospital were similar; there were no cases of in-hospital angina recurrence. Lacunar stroke developed in 2 patients of group 1, in both cases there was an initial neurologic deficit.

Thus, the results obtained indicate that the use of additional surgical techniques in CABG with the complete revascularization in patients with calcified lesions provides the same efficacy and safety as in standard CABG performed in patients with local coronary artery stenosis without calcification. This is at odds with the data demonstrated by Ertelt K, et al. (2013) [4] and Bourantas CV, et al. (2015) [7]. In these studies, calcification was assessed using angiography without the use of MSCT. However, coronary angiography had a higher specificity, but lower sensitivity compared to MSCT in determining CAC. MSCT coronary angiography, being a non-invasive diagnostic method, has both high sensitivity and high specificity for calcification detection. In a relatively small sample (n=48), we noted significantly higher efficacy contrast-enhanced and non-contrast-enhanced MSCT for describing the distal areas of calcified arteries. One way or another, both methods have pros and cons, therefore, in difficult and doubtful cases, we consider it important to use them together. We propose the inclusion of MSCT in the list of necessary tests in cases when an invasive treatment is planned for a patient with CAC.

The current study has a short-term follow-up period. Undoubtedly, further study with the assessment of long-term outcomes is required. The problem as a whole requires a broader consideration: so far, no randomized multicenter trials have been conducted and there are no practical guidelines for managing this category of patients.

Conclusion

CABG in CAC involves more frequent use of complex reconstructive surgical interventions, endarterectomies, anastomoses with small coronary arteries compared to standard CABG. The complete myocardial revascularization in patients with calcification achieved with these techniques provides in-hospital outcomes similar to those in patients without distal CAC.

Relationships and Activities. The study was performed within the research work № 81 under the State Assignment № AAAA-A18-118022290040-7.

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Comparison of Cardiopulmonary Exercise Capacity in Patients with Atrial Septal Defect Treated with Minimally Invasive Cardiac Surgery or Transcatheter Closure

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Aim. The main aim of our study was to compare the results of transcatheter atrial septal defect (ASD) closure versus minimally invasive cardiac surgery (MICS) focusing on cardiopulmonary exercise capacity and echocardiographic findings preoperatively and 1 month after defect closure.

Material and methods. 54 patients with ASD and finally 43 patients who were followed up were included in the study. 21 patients were in MICS (robotic or endoscopic approach) and 22 patients were in transcatheter closure arm. All patients investigated in detail by transesophageal echocardiography and underwent cardiopulmonary exercise test (CPET). At the end of first month, CPET and transthorasic echocardiography were reperformed.

Results. There was significant improvement of physical capacity after 1 month following the transcatheter closure procedure documented by exercise time and VO_2 max. Tricuspid annular plane systolic excursion (TAPSE) and tricuspid lateral annular systolic velocity (Tri S) were not changed. In surgery group right heart diameters declined significantly; but VO_2 max, TAPSE and Tri S significantly decreased.

Conclusion. Cardiopulmonary exercise function is increased in transcatheter closure group 1 month after closure and contrary not in MICS group. This may be caused by long recovery time of the right ventricle after surgery. Device closure of ASD is preferable to surgical closure if the anatomy is suitable. However, MICS for ASD closure is safe, with short recovery period and less scarring.

Key words: atrial septal defect, cardiopulmonary exercise test, minimally invasive surgical procedures, transcatheter closure.

Relationships and Activities: none.

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ASD — atrial septal defect, AT — anaerobic threshold, CPBT — cardiopulmonary bypass time, CPET — cardiopulmonary exercise test, EF — ejection fraction, MICS — minimally invasive cardiac surgery, PAPs — pulmonary artery systolic pressure, RA — right atrium, RER — relative exchange ratio, RV — right ventricle, TAPSE — tricuspid annular plane systolic excursion, TEE — transesophageal echocardiography, TTE — transthorasic echocardiography, Tri S — tricuspid annular systolic velocity, XCT — aortic cross-clemping time, VE — ventilatory efficiency, VO_2 max — maximal oxygen consumption.

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Atrial septal defect (ASD) of secundum type is one of the most common forms of congenital heart disease in adults. ASD results in additional flow through the right atrium (RA), the right ventricle (RV), and the pulmonary circulation. This is usually well tolerated for a prolonged period of time. The diagnosis is frequently made in adulthood. The most common presenting symptoms at adult age are palpitations, exertional dyspnea or fatigue, which increases with age [1]. Closure of atrial septal defects either percutaneously or surgically is indicated in patients with a hemodynamically significant shunt that causes enlargement of the right heart [2]. Complications include atrial arrhythmia, RV failure, and pulmonary arterial hypertension (PAH) if not repaired by early adulthood [1]. When RV is no more than moderately dilated before closure, there is little concern about persistent clinically relevant RV dysfunction. Additionally, while most patients have resolution of RV dilation, it may persist and maximal exercise capacity may remain impaired in long term follow-up, in a sizable subset of patients [3].

Surgical treatment of ASD has been practiced for over fifty years and appears to be a safe and effective procedure. Surgical treatment of ASD could be through median sternotomy, small thoracotomy with endoscopic support and with robotic assistance. Transcatheter closure of ASD with the ASD Septal Occluder has become a feasible alternative to conventional surgical closure in selected patients [4]. Transcatheter closure has the advantage of avoiding the need for sternotomy, cardiopulmonary bypass and intensive care stay, facilitates rapid patient recovery and confers financial returns. There are some limitations for transcatheter ASD closure such as anatomical and device-related. Main limitations to transcatheter ASD closure may be insufficient surrounding rims, primum or sinus venosus-type defects, multiple or associated defects and excessively bulging atrial septal aneurisms (ASA).

There are only a few studies comparing the results of surgical and transcatheter ASD closure [5-7]. The main aim of our study was to compare the results of transcatheter ASD closure versus minimally invasive cardiac surgery (MICS) focusing on cardiopulmonary exercise capacity and echocardiographic findings preoperatively and 1 month after defect closure.

Material and methods

Study population. We prospectively included 54 patients with ostium secundum ASD in our institution between September 2018 and July 2019. This study protocol was approved by the local ethics committee and informed consent was obtained from all individual participants. They underwent closure, either surgical or transcatheter using the Amplatzer Septal Occluder (ASO). Patients with coronary heart disease, moderate or severe valvular heart disease, pulmonary vascular resistance greater than two thirds of systemic vascular resistance, defect size >40 mm, other congenital heart disease and those unable to exercise were excluded. Patients with small ASD with a left-to-right shunt (Qp/Qs) of less than 1,5:1, sinus venosus ASD including partial anomalous pulmonary venous drainage, who did not have enlargement of the right heart diameters or pulmonary hypertension at rest and during exercise, without clinical symptoms of heart failure and without paradoxical embolism, did not receive an ASD closure in accordance to AHA guidelines [8]. 11 patients who did not undergo cardiopulmonary exercise test at first month were excluded from the study. Consequently, we included totally 43 patients; 21 patients who had surgery and 22 patients who had transcatheter closure.

All patients with ASD were investigated in detail by transesophageal echocardiography (TEE). Cases of ASD with a TEE diameter of 30 mm or less with a septal rim of at least 5 mm and non-floppy were considered suitable for transcatheter closure. Patients who objected for percutaneous closure, those who had single defect too large for occlusion and multiple defects unsuitable for interventional closure were randomized to surgery. All patients underwent to cardiopulmonary exercise test (CPET). At the end of first month CPET and transthoracic echocardiography (TTE) were reperformed.

Surgical closure. The minimal invasive endoscopic approach or Da Vinci SI robotic surgery system (Intuitive Surgical, Inc, Sunnyvale, CA, USA) without sternotomy was used. For minimal invasive endoscopic approach, the main working port and port for surgical endoscope were placed with skin incision. For Da Vinci SI robotic surgery, mini-thoracotomy was used for pericardiotomy, deployment of cardioplegic cannula, left ventricular drainage by using of the instruments and 3D-endoscope of da Vinci complex and assistant's work during the main surgical stage. In our cohort 7 patients were undergone port access endoscopic approach and 14 patients were undergone robotic surgery.

Transcatheter closure. Transcatheter closure of ASD using an Amplatzer Septal Occluder device (AGA Medical Corporation; Plymouth, MN, USA) was performed under general anesthesia with the assistance of TEE. Hemodynamic evaluation was performed before ASD closure. An exchange guide wire was placed in a left pulmonary vein. The appropriate size device was then screwed on the cable and advanced inside the proper size sheath. Its position as well as stability was assessed by fluoroscopy and TEE. All patients were instructed about infective endocarditis prophylaxis for six months after device placement. Aspirin 81-100 mg and clopidogrel was initiated 48 h before closure and continued for three months thereafter.

Echocardiography. Measurements of LV and RV internal dimensions obtained according to American Society of Echocardiography recommendations with an Epic 7 Ultrasound System (TTE Philips Healthcare, Andover, MA). To minimize inter-observer and intra-observer variations, one trained person performed all examinations. Two measurements of the RV were made in the apical four-chamber view: RV short-axis dimension (RV1), defined as the maximal dimension from the right septal surface to the free wall perpendicular to the long axis; and maximal RV long-axis dimension (RV2), defined as the distance between the RV apex and the mid-point of the tricuspid valve. RA was measured as apicobasal (RA1) and mediolateral (RA2) from apical four-chamber view. All patients were in normal sinus rhythm. In every patient the pulmonary-to-systemic flow ratio (Qp/Qs) was calculated, and right ventricular systolic pressure (RVSP) was measured in patients with tricuspid valve regurgitation using the simplified Bernoulli formula. All patients underwent TEE to characterize the ASD, measure the maximal ASD diameter and the surrounding rims.

Cardiopulmonary exercise test (CPET). A total of 54 patients with ASD had a treadmill exercise ergospirometry test based on a Bruce protocol (Ergometrics 900, Ergoline, Bitz, Germany). Breath-to-breath measurements of expired gas values were analysed. Heart rate, blood pressure and ventilation were recorded continuously during ergospirometry. We measured ventilatory flow, inspiratory and expiratory oxygen concentration difference, expiratory carbon dioxide concentration. From these variables oxygen uptake, peak oxygen uptake, carbon dioxide delivery, respiratory exchange ratio (RER) and ventilatory equivalents for oxygen and carbon dioxide (VE/VO_2, VE/VCO_2) were calculated by machine. Patients were encouraged to exercise to exhaustion or to a respiratory exchange ratio ⩾1,0. VO_2 max was defined as the amount of oxygen consumed by the body at the peak of tolerable exercise. The anaerobic threshold (AT) was determined from the plot of carbon dioxide output (VCO_2) against oxygen uptake (VO_2), where the slope of this linear relation increased owing to a rise in VCO_2 (V-slope method); or VO_2 at the onset of blood lactate accumulation. At this time, there is a significant increase in blood lactate concentration. VE/VO_2 and VE/VCO_2 was defined as ventilator efficiency [9].

Statistical Analysis. Statistical analysis was made using the computer software Statistical Package for Social Sciences (IBM SPSS Statistics for Windows, version 21.0. released 2012, IBM Corp., Armonk, New York, USA). Fisher's exact test and Pearson chi-square analysis were performed for categorical variables. Fitness to normal distribution was analyzed with the Shapiro Wilk test. Data was expressed as "mean±standard deviation (SD)" for variables with normal distribution, "median (15^{th}-75^{th})" for variables without normal distribution and "n (%)" for categorical variables. Mann-Whitney U test was used for comparing quantitative variables with abnormal distribution while Student t-test was used for comparing the means between two groups with normal distribution. Paired sample t test was used for related samples with normal distribution while Wilcoxon matched-pair signed rank test was used for related samples with skewed distribution. A p-value <0,05 was considered statistically significant.

Results

Among 54 patients with ASD, 43 patients who were followed up were included in the study. Patients' demographic, echocardiographic and exercise data are summarized in Table 1. Median age in 21 patients undergoing MICS was 34 (24-49) with 52,4% being female; whereas in 22 patients undergoing transcatheter closure the median age was 51 (32-57) with 63,6% being female. In surgery group 1 patient was hypertensive, 1 patient was diabetic; in closure group no patient was diabetic, 5 patients were hypertensive. The median ASD size was 20 (18-28) mm in surgery group and 16,5 (14-20) mm in transcatheter group. The size of the ASD was larger and the Qp/Qs ratio was higher in the MICS group; because patients with large ASD were not suitable for transcatheter closure and were referred to surgery. VO_2 max was higher in MICS group. No clinical or statistical differences were found in echocardiography and cardiopulmonary functional capacity parameters between MICS and transcatheter closure group except for RV and VO_2 max. Total cardiopulmonary bypass time (CPBT) averaged 72,7±25,8 min and aortic cross-clamping time (XCT) was 31,7±13,08. The median diameter of implanted devices was 20 (18-28,5) mm.

Preoperatively VO_2 max (ml/kg/min) was 22,7±5,6 in MICS and 18,8±6,0 in transcatheter group. Exercise time was 472,2±132,3 in preoperative surgery group and 409,9±108,3 in another group.

Data obtained by TTE and cardiopulmonary exercise testing at baseline and 1 month after the procedure are summarized for two groups in Table 2 and 3.

Transcatheter closure group. There was a significant improvement of physical capacity after 1 month following the procedure documented by exercise time, VO_2 max, VO_2, VE (minute ventilation), and O_2 pulse (Table 2, Figure 1A). CPET at first month after the procedure demonstrated longer exercise time (405 (350-495) vs 465 (382,75-601,75) second p=0,02), increased maximal oxygen consumption (18,78±6,00 vs 20,37±6,45 p=0,014), increased VE from 50,45±17,44 to 56,77±18,6 L/min (p=0,016). And also, O_2 pulse (VO_2/HR) increased significantly from 10,43±2,54 to 11,27±3,35 ml (p=0,041). VE/VCO_2 slope which is important for prognosis didn't change in both groups. Heart rate (HR) at anaerobic threshold decreased in both groups. Right atrium, right ventricle, pulmonary artery pressure decreased after transcatheter closure significantly as expected. Tricuspid annular plane systolic excursion (TAPSE) and tricuspid lateral annular systolic velocity (Tri S) were not changed but were both in normal range. There was no difference in left ventricular ejection fraction in either group. One patient in transcatheter arm had acute atrial fibrillation postoperatively and returned to sinus rhythm spontaneously.

Surgery group. Cardiopulmonary functional exercise and echocardiographic parameters before and 1 month later are shown in Table 3. Exercise time increased but it didn't reach statistically significance. VO_2 max decreased from 22,6±5,57 to 19,9±5,11 ml/kg/min (p=0,006) (Figure 1B). In accordance with this, TAPSE (23,9±3,49 vs 16,71±3,57 p<0,001) and Tri S (13 (12-15) vs 10,0 (10-11) p<0,001) significantly decreased. Worsening of the right ventricle function can explain the deterioration of CPET parameters in surgery group. Right heart diameters and PAPs declined meaningfully. 1 patient underwent to reoperation for pericardial effusion in MICS group and the follow up was uneventful.

Table 4 compares the changes in CPET and echocardiographic parameters in surgical and transcatheter groups at 1-month follow-up. There were significant differences in VO_2 max and right ventricle parameters between the surgical and percutaneous groups.

Discussion

This prospective study provides evidence that VO_2 max, which is an important indicator of exercise capacity, is increased in transcatheter closure arm 1 month after closure. On the contrary cardiopulmonary and right ventricle functions were decreased in MICS group at first month evaluation. This reduction can be explained by the fact that one month is too short to recover from surgery. At first month, the general condition of the patients in surgical group was good and wound healing was achieved due to having minimally invasive surgery. Symptomatic improvement was seen in all patients and the follow-up period was uneventful. Exercise time was also increased in surgery group, but was not statistically significant. These results suggest that cardiopulmonary exercise functions may be better in the surgical group if the exercise test was performed 6 months or 1 year after surgery. The lack of increase in VO_2 max at first month does not translate to absence of improvement in ASD patients undergone surgery. Furthermore, left ventricle and left atrium diameters increased non-significantly after closure or surgery, due to increased volume loading of the LV, as well as to an improved ventricular interaction. In our study ASD size and Qp/Qs were greater in MICS group which may cause bias; however, in order to avoid bias, we compared the groups among themselves and compared the changes between both groups.

Currently the transcatheter closure of ASD is common practice. Its main advantages are, absence of a surgical scar, shorter hospitalization time and being able to avoid general anesthesia [10, 11]. Study results of Komar M, et al. demonstrate that device closure of ASD in the elderly is technically easy, safe, and has minimal complications [12]. However, complications associated with this procedure for atrial septal defects have been reported including device embolization, thrombosis, device malposition, and cerebrovascular events. In a previous study including 30 patients, it was shown that transcatheter closure was safe and effective treatment for atrial septal defects and could be an alternative option to open heart surgery [13]. Additionally, echocardiographic data demonstrated a decrease in right ventricular and right atrium area, suggesting that atrial septal occlusion improved volume overload of the right heart [13]. In a recently published meta-analysis of Mylonas KS, et al., authors concluded that MICS constitutes a viable alternative to transcatheter repair and should be considered as an option for hemodynamically significant ASDs [14]. According to data published in 2018 by Prochownik P, et al., improvement of right heart chambers was observed already after 1 month following the transcatheter procedure. At 24-month follow-up higher maximal oxygen consumption was evident [15]. In contrast, Helber U, et al. observed an increase in VO_2 max only after 10 years, and no notable effects within the first 4 months in ASD patients undergone surgical closure, as in our study [16].

Several trials indicated a significant reduction of PAPs and improvement of exercise capacity after correction of ASD. In patients with elevated pulmonary vascular resistance and irreversible damage to the pulmonary arterioles might prevent the improvement of postoperative exercise capacity in patients with left to right shunt and high pulmonary arterial pressure. In a study of Kobayashi et al. there was a significant negative correlation between

Table 1

Baseline, demographic, echocardiographic and cardiopulmonary exercise test data for patients in surgical and transcatheter closure groups

	MICS group n=21	Transcatheter closure n=22	p
Age	34 (24-49)	51 (32-57)	0,068
Gender (female)	52,4 (11)	63,6 (14)	0,455
NYHA			0,745
1	28,6 (6)	31,8 (7)	
2	33,3 (7)	40,9 (9)	
3	38,1 (8)	27,3 (6)	
DM	4,8 (1)	0	0,488
HT	4,8 (1)	22,7 (5)	0,103
ASD device size		20 (18-28,5)	
CPBT	72,7±25,8		
XCT	31,7±13,08		
ASD size	20 (18-28)	16,5 (14-20)	0,004
Qp/Qs	2,5 (2,0-3,0)	1,8 (1,7-2,2)	0,005
PAPs	40 (35-45)	35 (30-40)	0,284
RA1	43±6	41±7	0,558
RA2	49±8	48±9	0,654
RV1	44 (37-46)	40 (37-49)	0,618
RV2	69±7	64±5	0,014
TAPSE	25 (20-26)	24 (20-25)	0,278
Tri S	13 (12-15)	13 (12-14)	0,939
LA	33±4	35±4	0,066
LVESD	25 (23-27)	27 (25-30)	0,083
LVEDD	42±6	43±4	0,672
EF	65 (65-65)	65 (60-65)	0,093
Exercise time	472,2±132,3	409,9±108,3	0,098
VO_2 (L/min)	1,6±0,46	1,44±0,36	0,208
VO_2 AT (ml/kg/min)	18,35±7,16	15,07±4,87	0,086
VO_2 AT%	82±17	81±14	0,793
VO_2 max (ml/kg/min)	22,7±5,6	18,8±6,0	0,034
VCO_2 (L/min)	1,59±0,45	1,40±0,44	0,184
RER	1,0±0,10	0,97±0,10	0,256
VE (L/min)	52±11	50±17	0,755
HR AT (beats/min)	138±17	124±23	0,033
HR peak (beats/min)	153±15	142±25	0,083
O_2 Pulse	10,2±3,1	10,4±2,5	0,762
VE/VCO_2 slope	30,4 (27,8-32,4)	31,4 (28,7-33,7)	0,337
$PETO_2$	114±7	116±7	0,310
$PETCO_2$	32±4	32±5	0,756
VE/VO_2	29,9±4,1	30,9±6,8	0,578
VE/VCO_2	29,9±3,4	31,8±6,2	0,228
VE/VO_2 AT	26,3 (25,1-28,0)	27,0 (22,6-30,4)	0,481
VE/VCO_2 AT	29,3 (26,0-30,7)	30,8 (26,9-33,0)	0,319

Note: data are expressed as mean ± standard deviation and median (interquartile range) or absolute number (percentage).

Abbreviations: ASD — atrial septal defect, CPBT — cardiopulmonary bypass time, DM — diabetes mellitus, EF — ejection fraction, HR — heart rate, HT — hypertension, LA — left atrium, LVESD — left ventricle end-systolic diameter, LVEDD — left ventricle end-diastolic diameter, min — minutes, NYHA — New York Heart Association, PAPs — pulmonary artery systolic pressure, RA — right atrium, RER — relative exchange ratio, RV — right ventricle, TAPSE — tricuspid annular plane systolic excursion, Tri S — tricuspid lateral annular systolic velocity, VE — ventilatory efficiency, VO_2 max — maximal oxygen consumption, VCO_2 — production of carbon dioxide, VE/VCO_2 — ventilatory equivalent for CO_2, VE/VO_2 — ventilatory equivalent for O_2, VO_2 AT — oxygen consumption in at anaerobic threshold, XCT — aortic cross-clamping time.

Table 2

Transthoracic Echocardiography and Cardiopulmonary Exercise Testing at Baseline and After Transcatheter Closure of Atrial Septal Defect (n=22)

	Baseline	1 month	p
Exercise time	405 (350-495)	465 (382,75-601,75)	0,002
VO_2 (L/min)	1,43±0,36	1,56±0,42	0,011
VO_2 AT (ml/kg/min)	15,06±4,87	14,42±4,65	0,415
VO_2 AT%	80,5 (70,5-94,25)	74 (61,25-86,0)	0,013
VO_2max (ml/kg/min)	18,78±6,00	20,37±6,45	0,014
VCO_2	1,39 (1,09-1,62)	1,52 (1,23-1,70)	0,015
RER	0,96±0,101	0,99±0,07	0,149
VE (L/min)	50,45±17,44	56,77±18,6	0,016
HR AT (beats/min)	135 (105,5-140,25)	117 (102-136)	0,273
HR peak (beats/min)	141,7±25,4	141,5±24,6	0,919
O_2 Pulse	10,43±2,54	11,27±3,35	0,041
VE/VCO_2 slope	31,4 (28,42-33,7)	31,5 (28,6-35,2)	0,404
$PETO_2$	115,8±6,98	115,71±7,28	0,957
$PETCO_2$	31,5±5,26	30,09±4,63	0,166
VE/VO_2	30,8±6,84	32,2±6,51	0,259
VE/VCO_2	31,78±6,18	32,5±6,51	0,417
VE/VO_2 AT	28,16±6,61	25,9±5,85	0,005
VE/VCO_2 AT	30,85±6,04	31,25±6,50	0,582
PAPs	36,7±6,31	28,9±7,19	<0,001
RA1	41,3±7,02	37,5±7,35	0,002
RA2	47,5 (40,0-53,0)	40 (39,25-49,25)	<0,001
RV1	40 (36,75-49,25)	36,5 (34,5-40,0)	0,001
RV2	64,5 (50-68)	60 (56,5-62,75)	<0,001
TAPSE	27,7±3,36	23,5±1,96	0,289
Tri S	13 (12-14)	13 (12-14	0,791
LA	35,05±4,06	34,6±4,02	0,609
LVESD	26,5 (25-30)	28 (26,5-31)	0,060
LVEDD	42 (40-45,25)	42 (40-45,25)	0,792
EF	65 (60-65)	65 (60-65)	0,914

Abbreviations: EF — ejection fraction, LA — left atrium, LVESD — left ventricle end-systolic diameter, LVEDD — left ventricle end-diastolic diameter, PAPs — pulmonary artery systolic pressure, RA — right atrium, RER — relative exchange ratio, RV — right ventricle, TAPSE — tricuspid annular plane systolic excursion, Tri S — tricuspid annular systolic velocity, VE — ventilatory efficiency, VO_2 max — maximal oxygen consumption, VCO_2 — production of carbon dioxide, VE/VCO_2 — ventilatory equivalent for CO_2, VE/VO_2 — ventilatory equivalent for O_2, VO_2 AT — oxygen consumption at anaerobic threshold, min — minutes.

Qp:Qs and peak VO_2, besides that exercise capacity in patients with large left-to-right shunt increased after surgical closure of ASD (mean 4,6±2,0 months) [17].

In transcatheter ASD closure group Dhillon R, et al. observed improvement of right ventricular functions 6-12-months after ASD closure [18]. In most patients the size of right heart chambers returned to normal in a 24-month follow-up, which was also shown in a study of Zhong-Dong ZD, et al. [19]. Stephensen SS, et al. said that elderly patients with diastolic dysfunction, larger shunts and sedentary people may need longer time to adapt to the new physiology; furthermore, patients with smaller shunts in their transcatheter closure series had larger improvement in predicted exercise capacity [20]. Santos M, et al. demonstrated the presence of distinctly abnormal RV and pulmonary vascular responses to exercise in a subset of patients after successful ASD closure, despite normal resting hemodynamics [21]. In another study ASD closure led to a significant reduction in stress-induced pulmonary hypertension and right heart diameters indicating reverse RV remodeling but the VO_2 max did not change after ASD closure [22]. Takaya Y, et al. evaluated short- and long-term benefits of transcatheter closure of ASD in patients older than 40 years and found that peak VO_2 did not change at 1 and 3 months, but it improved significantly after 6 months [23]. Suchon E, et al. compared surgical and

Table 3

Transthoracic Echocardiography and Cardiopulmonary Exercise Testing at Baseline and After Surgical Closure of Atrial Septal Defect (n=21)

	Baseline	1 month	p
Exercise time	482 (440-550)	491(419,5-580)	0,940
VO_2 (L/min)	1,5±0,45	1,43±0,42	0,013
VO_2 AT (ml/kg/min)	18,3±7,16	16,56±5,57	0,141
VO_2 AT%	84 (70,0-97,5)	81 (71-92)	0,687
VO_2 max (ml/kg/min)	22,6±5,57	19,9±5,11	0,006
VCO_2 (L/min)	1,5 (1,25-2,04)	1,46 (1,07-1,79)	0,117
RER	1,00±0,09	1,02±0,078	0,312
VE (L/min)	51,8±11,3	48,1±12,4	0,069
HR AT (beats/min)	139 (124,5-153,5)	125 (107-141)	0,028
HR peak (beats/min)	153,1±15,4	143,3±19,9	0,003
O_2 Pulse	10,1±3,14	16,6±30,6	0,331
VE/VCO_2 slope	30,4 (27,7-32,6)	29,9 (27,1-31,4)	0,192
$PETO_2$	113,7±6,6	114,3±7,86	0,662
$PETCO_2$	32,0±3,97	31,3±5,89	0,523
VE/VO_2	29,9±4,07	29,9±4,78	0,976
VE/VCO_2	29,9±3,44	29,16±3,98	0,326
VE/VO_2 AT	25,9±4,19	26,44±5,56	0,763
$VEVCO_2$ AT	28,6±4,11	28,68±4,31	0,990
PAPs	38,9±8,12	27,28±5,93	<0,001
RA1	42,5±6,33	36,6±6,46	<0,001
RA2	50 (45-55)	42 (38-46,5)	<0,001
RV1	44 (36-47,5)	37 (33-40)	0,002
RV2	68 (66-74,5)	63 (58-69)	0,001
TAPSE	23,9±3,49	16,71±3,57	<0,001
Tri S	13 (12-15)	10,0 (10-11)	<0,001
LA	32,7±4,01	33,52±4,61	0,420
LVESD	25,0 (23-28)	25,0 (23-28)	0,560
LVEDD	41 (39-45,5)	43 (41-45,5)	0,432
EF	65 (65-65)	65 (60-65)	0,066

Abbreviations: EF — ejection fraction, LA — left atrium, LVESD — left ventricle end-systolic diameter, LVEDD — left ventricle end-diastolic diameter, PAPs — pulmonary artery systolic pressure, RA — right atrium, RER — relative exchange ratio, RV — right ventricle, TAPSE — tricuspid annular plane systolic excursion, Tri S — tricuspid annular systolic velocity, VE — ventilatory efficiency, VO_2 max — maximal oxygen consumption, VCO_2 — production of carbon dioxide, VE/VCO_2 — ventilatory equivalent for CO_2, VE/VO_2 — ventilatory equivalent for O_2, VO_2 AT — oxygen consumption at anaerobic threshold, min — minutes.

ASO (Amplatzer septal occlusion) groups at 1-year follow up and indicated that VE/CO_2 slope decreased more in the ASO than in the surgical group [24]. Despite increased VE/VCO_2 slope has been proven to be a strong predictor of mortality, we couldn't see statistically difference in our analysis. This may be due to early evaluation of postoperative patients with cardiopulmonary exercise test.

Limitations. The major limitation of our study is, short follow-up period. We aimed to include defect size and functional capacity matched groups, however there was difference between two groups due to referring patients with bigger ASD size to surgery in clinical practice. Ventricle function and functional capacity could be better estimated if study data was supported by catheterization, magnetic resonance imaging and strain. Another limitation was a relatively small sample size.

Conclusion

To the best of our knowledge, our study is rare in its use of cardiopulmonary exercise functions before and after ASD closure comparing transcatheter closure and minimally invasive

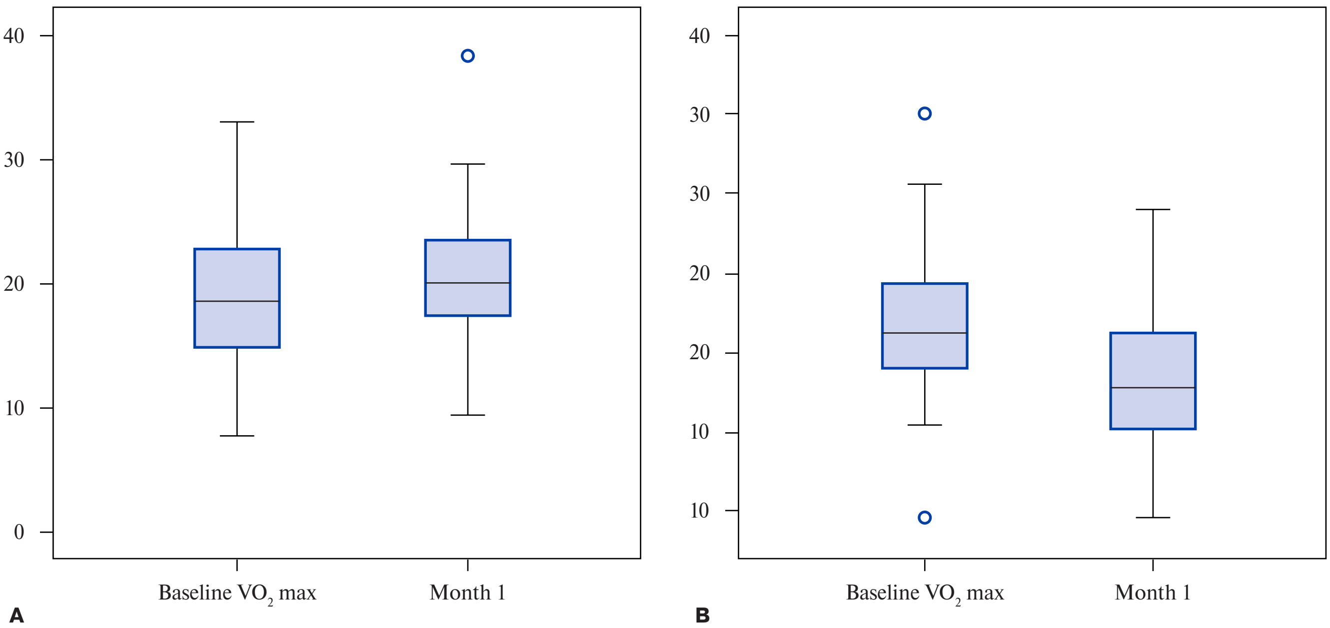

Figure 1. Box-plot representations of maximal VO_2 (ml/kg/min) at baseline and 1 month after procedure in transcatheter (**A**) and minimal invasive surgery (**B**) groups.

Table 4

Comparison of changes in CPET and echocardiographic parameters in the surgical and transcatheter groups at 1-month follow-up

	MICS group	Transcatheter closure	p
VO_2 (L/min)	-0,17±0,28	0,13±0,21	<0,001
VO_2 AT (ml/kg/min)	-1,78±5,32	-0,64±3,61	0,419
VO_2 AT%	0,00 (-9,0 — 6,0)	-7,0 (-12,0 — 0,0)	0,145
VO_2 max (ml/kg/min)	-2,67±3,98	1,59±2,77	<0,001
VCO_2 (L/min)	-0,10 (-0,30 — 0,06)	0,15 (-0,03 — 0,35)	0,005
O_2 Pulse	6,43±29,58	0,84±1,80	0,381
VE/VCO_2 slope	-0,87±3,48	0,92±4,63	0,160
$PETO_2$	0,95±9,29	-0,10±8,05	0,706
RA1	-5,86±4,0	-3,82±4,94	0,146
RA2	-7,0 (-10,0 — -4,0)	-3,0 (-5,0 — -2,0)	0,100
RV1	-4,0 (-10,0 — -2,0)	-4,0 (-6,0 — -0,0)	0,341
RV2	-8,0 (-10,0 — -4,0)	-4,0 (-5,0 — -2,0)	0,025
TAPSE	-7,19±4,85	0,82±3,53	<0,001
Tri S	-3,0 (-5,20 — -1,0)	0,0 (0,0-0,0)	<0,001

Abbreviations: RA — right atrium, RV — right ventricle, TAPSE — tricuspid annular plane systolic excursion, Tri S — tricuspid annular systolic velocity, VE — ventilatory efficiency, VO_2 max — maximal oxygen consumption, VCO_2 — production of carbon dioxide, VE/VCO_2 — ventilatory equivalent for CO_2, VO_2AT — oxygen consumption at anaerobic threshold, min — minutes.

cardiac surgery. Cardiopulmonary exercise function is increased in transcatheter closure group 1 month after closure and contrary not in MICS group. This may be caused by long recovery time of the right ventricle after surgery. We suggest that device closure of ASD is preferable to surgical closure if the anatomy is suitable. However, MICS for ASD closure is safe, with short recovery period and less scarring. Additionally, minimally invasive cardiac surgery may be preferred over sternotomy; due to shorter hospital stay, rapid recovery and lack of sternotomy in ASD patients unsuitable for transcatheter closure.

Relationships and Activities: none.

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Bilateral injury of deep peroneal nerve in the patient after heart transplant

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In March 2015, a 62-year-old patient with advanced heart failure underwent a failed radiofrequency ablation, followed by paresis of muscles in the anterior compartment of the leg. After rehabilitation, partial recovery of the paresis was achieved. Orthotopic heart transplantation was performed 9 months after ablation at the at the Institute of Cardiology, followed by a bilateral paresis of muscles in the anterior leg compartment. Rehabilitation was implemented. The possible cause of paresis is most likely to be due to food shortages, mainly related to a folic acid deficiency.

Key words: heart transplantation, bilateral peroneal nerve paralysis.

Relationships and Activities: none.

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Clinical situation

In September 2015, a 62-year-old patient with dilated cardiomyopathy, NYHA class III heart failure (HF), left ventricular ejection fraction (LVEF) of 44%, severe mitral regurgitation, history of asystole in 2012, followed by implantation of a cardioverter-defibrillator was admitted to the National Institute of Cardiology. Since 2010, ventricular tachycardia is observed. There was a failed radiofrequency ablation in March 2015, followed by palsy of lower limb extensor muscles (Fig. 1A, B, C). Physiotherapy was carried out, after which the muscle function gradually recovered. Later, a thrombus on the cardioverter lead was detected, which required the administration of oral anticoagulants.

In mid-November 2015, HF exacerbation was recorded.

On December 23, 2015, a heart transplant was performed at the National Institute of Cardiology.

On the 5th day after surgery, palsy of muscles in anterior compartment of the leg was recorded. On day 13, the patient was examined by a neurologist, who revealed normal, symmetrical reflexes in the lower extremities without sensory disturbances. Hypotrophy of the lower limb muscles was noted. Neurologist supposed that a possible cause of palsy is fibular nerve compression at the fibula head. Electrical stimulation of the fibular nerves was ordered.

In parallel with postoperative rehabilitation, physiotherapy was carried out aimed at recovering the fibular nerve function. Despite the improvement of neuromuscular transmission, the full restoration of the feet functional activity was not achieved.

The ability to walk with walkers became possible only on the 52nd day after treatment. The patient's gait had typical features of fibular nerve palsy, which was also characterized by forward inclination of body while walking with walkers.

This type of gait did not appear immediately, but during walking.

On the 57th day after heart transplant, levels of vitamin B12 and folic acid were determined due to

A

B

C

Figure 1 (A, B, C). Bilateral injury of deep peroneal nerve. Falling feet.

persistent high-colour-index anemia. According to results, vitamin B12 levels were normal, but folic acid values were reduced (2,58 ng/ml with acceptable values of 4,6-18,7 ng/ml).

On the 125th day after heart transplant, the patient was discharged with recommendations to continue rehabilitation at home. On October 17, 2017, the patient was rehospitalized for a second postoperative examination, control of laboratory and instrumental tests. The patient was cachectic and moved with walkers or elbow crutches. There was a permanent paresis of mentioned muscles of both lower limbs. According to the patient, a full course of rehabilitation was performed, including kinesiotherapy and physiotherapy.

Discussion

Bilateral peroneal nerve paralysis after cardiac surgery is a very rare case described in the literature [1]. The dysfunction is occurred due to a partial or complete nerve impairment, followed by leg muscle dysfunction. Paresis is the result of deep peroneal nerve injury. The compensating gait was typical: in order not to touch the ground with the toe, the patient raises his leg high, and when lowering it, first touches the ground with the toe, then the outer edge of the foot and finally the sole. In addition, there was a forward inclination of body while walking with walkers.

On the lower extremity, unilateral paralysis of branches of the common peroneal nerve is most often observed, the most common cause of which is the compression of it by the fibula head. According to literature data, there is a description of one case with similar characteristics obtained by us [2].

One of the possible reasons for paresis after heart transplant could be mechanical compression during surgical positioning, as well as low body and limb weight, which is associated with more superficial location of the common peroneal nerve and its branches. However, it should be remembered that compression by fibula head often leads to injury of the common peroneal nerve, which will cause clinical symptoms related to both the superficial and deep branches [3]. But in this patient, the symptoms of deep branch injury were determined.

The second cause of paresis can be an ischemic stroke. However, strokes and vascular disorders of the central nervous system most often is associated with unilateral symptoms. Clinical manifestations in this patient indicates peripheral nerve injury, but not central.

Also, intervertebral disc disease can be considered the cause of paresis of deep peroneal nerve. But the given patient did not have this pathology, and such a disorder is often manifested by unilateral symptoms.

Nerve injury due to metabolic diseases (diabetes) can also often occur. But this patient was not diagnosed with metabolic diseases (diabetes) [4].

The injury of peripheral nerves as a result of vitamin or mineral deficiency is of great clinical importance for the formation of bilateral peroneal nerve paresis. In favor of this opinion, folic acid levels are indicated.

Folic acid is an indispensable vitamin for the synthesis of nucleic acids (DNA), the deficiency of which can cause nerve injury. Long duration of HF and cachexia could lead to changes in cell membranes, and folic acid deficiency could aggravate this process, which could also cause peroneal nerve paresis. The only argument against this is the absence of data on folic acid levels before surgery and there is no detection of nerve injury before cardiac ablation.

Conclusion

There are many possible causes that can lead to nerve injury. One of the most likely causes is folic acid deficiency. Despite the treatment and rehabilitation measures, the condition of the presented patient did not improve. One of the ways to prevent such a complication is the enhanced laboratory tests at the admission and preparation for surgery, as well as systematic monitoring after surgery, systematic rehabilitation and high compliance of patient are the only factors that are necessary for the rapid recovering.

Perhaps, due to the difficulties of postoperative complications, the use of immunosuppressive drugs, including tacrolimus, and the too short observation and treatment period did not lead to positive dynamics.

Relationships and Activities: none.

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