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K.V. Rudenko, V.V. Lazoryshynets, O.M. Trembovetska, L.O. Nevmerzhytska, M.O. Tregubova, P.A. Danchenko[1]
Amosov National Institute of Cardiovascular Surgery NAMS of Ukraine
[1]Bogomolets National Medical University

THE RESULTS OF SURGICAL TREATMENT OF PATIENTS WITH HYPERTROPHIC OBSTRUCTIVE CARDIOMYOPATHY AS A RISK FACTOR OF SUDDEN CARDIAC DEATH

e-mail: polinadanchenko12@gmail.com

The study includes 250 consecutive symptomatic patients with hypertrophic obstructive cardiomyopathy who underwent surgical extended myectomy, resection of anomalous chordal structures, mobilization of the papillary muscles and plication of the anterior mitral valve leaflet. The purpose of the study is to analyze the effectiveness of this technique and the immediate results of surgical correction. The results showed a statistically significant decrease of systolic pressure gradient on the left ventricular outflow tract, mitral regurgitation and an improvement in NYHA functional class. Sudden cardiac death (SCD) risk stratification was performed in 235 patients. The results of the study showed that the multi-stage correction allows to influence all links of pathological manifestation of the disease, but the question is how to predict the risk of SCD in already operated patients and how to protect them from life-threatening events?

Key words: hypertrophic cardiomyopathy, extended septal myectomy, surgical correction, sudden cardiac death

The work is a fragment of the research project "To improve the system of primary and secondary prevention of sudden cardiac death in patients with hypertrophic cardiomyopathy", state registration No. 0119U002019.

Hypertrophic cardiomyopathy (HCM) was initially described in living patients in 1959 by Morrow and Braunwald in a case series of 3 patients [10]. HCM is the most common sudden cardiac death (SCD)-related cardiomyopathy. The long-standing estimated prevalence has been 1 in 500 [7], with one study estimating the prevalence as high as 1 in 200 [14]. HCM is one of the most common causes of SCD in young athletes [5, 8].

In Ukraine, SCD statistics, both among general population and young people and athletes, remain uncertain. However, taking into account the prevalence of the disease (1:500 cases), the estimated number of patients with both obstructive and non-obstructive forms of HCM is about 75 thousand people.

The program on the study of the features of HCM diagnostics and treatment was established at the Amosov National Institute of Cardiovascular Surgery NAMS of Ukraine in 1993 when different methods of HCM treatment were applied. In the period from 1993 to 2019 there were applied and studied practically all invasive and non-invasive methods of HCM correction: dual-chamber (DDD) pacemaker implantation, classic Morrow technique, Bokeria-Borysov surgery, isolated mitral valve (MV) replacement, MV replacement with myotomy-myectomy, alcohol septal ablation (ASA). According to the analysis of the early and long-term results, implantation of dual-chamber pacemaker has shown its ineffectiveness and is now compared with placebo effect [9]. In addition, a considerable number of postoperative complications has attracted our attention in the surgical treatment group (iatrogenic complete AV block, iatrogenic defect of the interventricular septum (IVS), as well as damage of the aortic valve (AV) leaflets).

In view of the above, we are faced with the question of finding the optimal surgical treatment of HCM, which would be characterized by a minimal level of postoperative complications and, at the same time, high efficiency in reducing the risk of SCD.

In 2016, we implemented and completed the method of treatment of patients with HCM, proposed by Italian cardiac surgeon Paolo Ferrazzi (Monza, Italy), which presents a comprehensive multi-stage surgical approach to the HCM treatment.

The purpose of the work was to investigate the effectiveness of this technique, as well as to explore the early results of surgical correction in patients with obstructive HCM.

Materials and methods. The study included 250 consecutive symptomatic patients with obstructive HCM who underwent surgical extended myectomy, resection of the anomalous chordal structures, mobilization of the anterior and posterior groups of papillary muscles (PM) and plication of the anterior mitral leaflet (AML) in a period from 2016 to 2019.

The inclusion criteria for surgical treatment involved: systolic pressure gradient (SPG) on the left ventricle outflow tract (LVOT) ≥50 mmHg at rest or on physical exertion (or Valsalva maneuver) as well as heart failure symptoms resistant to medical therapy. Clinical features of 250 patients who were included to the study are presented in table 1.

Table 1

Baseline characteristics of 250 examined patients

Parameters (N of patients = 250)	
Demographic data	
Age (years), mean±SD (median)	50.1±14.7(54)
Males, n (%)	126 (50.4)
Clinical features	
NYHA functional class III or IV, n (%)	93 (37.2%)
Previous ASA, n (%)	16 (6.4%)
Paroxysmal or persistent AF, n (%)	32 (12.8)
Pre-operative echocardiographic data	
SPG on LVOT at rest or on exertion, mmHg (mean±SD)	92.8±30.7
Moderate or severe MR, n (%)	182 (72.8%)
AF – atrial fibrillation; ASA – alcohol septal ablation; LVOT – left ventricle outflow tract; MR – mitral regurgitation; NYHA – New York Heart Association; SD – standard deviation; SPG – systolic pressure gradient.	

For the purpose of SCD risk stratification and according to the European Society of Cardiology (ESC) guidelines on HCM treatment all patients older than 16 years old mandatory underwent HCM SCD risk calculation in a 5-year period with the help of calculator developed by ESC (HCM risk-SCD calculator) [9]. According to the guidelines, patients with HCM were divided into 3 groups accordingly: low-risk group (SCD risk <4%), moderate-risk group (SCD risk ≥4 and <6%) and high-risk group (SCD risk ≥6%). In-hospital mortality included any death within 30 days after surgery.

An important component of preoperative planning in the adult group was routine computed tomography (CT) imaging with contrast and CT angiography or MRI with gadolinium (fig. 1A, 1B). In case of anomalies or coronary artery lesions, patients were referred for cardiac catheterization. In the children's group, a CT or MRI study was performed with gadolinium with subsequent calculations of the size of the right ventricle (RV), left ventricle (LV) and IVS to detect structural abnormalities, degree of fibrotic process and congenital heart defects.

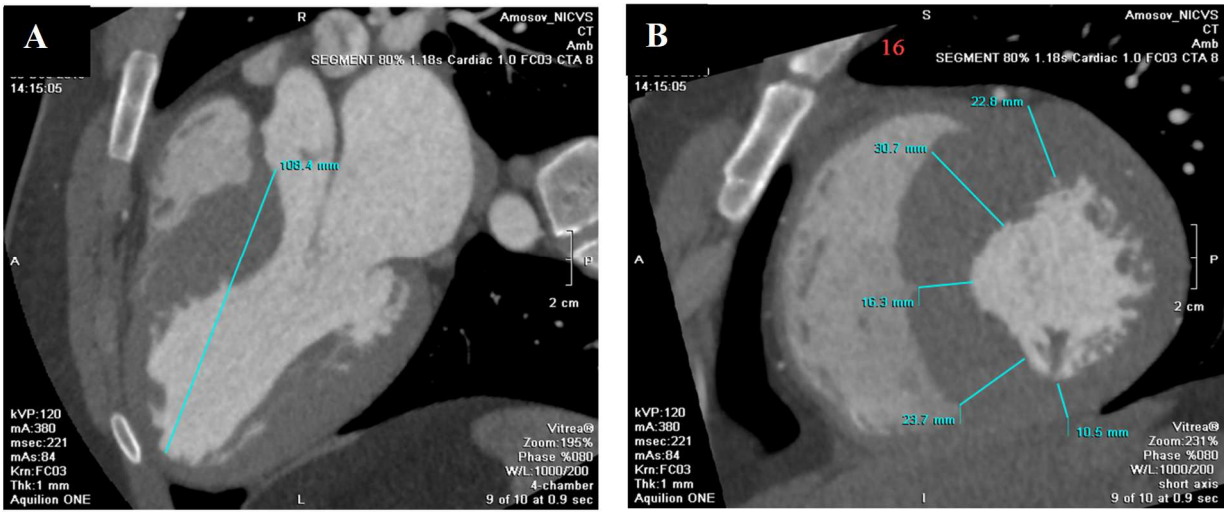

Fig. 1. Mandatory preoperative CT planning where the distance from the aortic annulus to the apex of the LV (LV depth) (A) and the dimensions of the LV and IVS at a distance of every 8 mm from the aortic annulus along the short axis are measured (B)

Surgical correction included a series of several mandatory steps: extended myectomy, resection of anomalous chordal structures of the MV, PM mobilization and, in case of necessity, AML plication with reduction of its area.

After induction of anesthesia, intraoperative transesophageal echocardiography (TEE) was performed to determine the extent of myectomy, as well as to assess the morphology of the MV and the presence of associated primary MV anomalies. TEE was repeated in the operating room immediately after stopping the cardiopulmonary bypass for the assessment of residual gradient on the LVOT and regurgitation on aortic and mitral valves, as well as for the detection of possible surgical complications such as iatrogenic perforation of the IVS or coronary fistula (fig. 2A, 2B).

Septal myectomy (often referred to as "extended myectomy" in modern literature) was performed during cardiopulmonary bypass with mild general hypothermia. Using the exposure through the oblique aortotomy the myectomy was begun from two longitudinal incisions in the basal part of the IVS, 2-3 mm below the AV, gradually continuing the resection more distally, to the base of the PM (equatorial zone), creating a trapezoidal muscular band which is wider towards the apex than at the subaortic level.

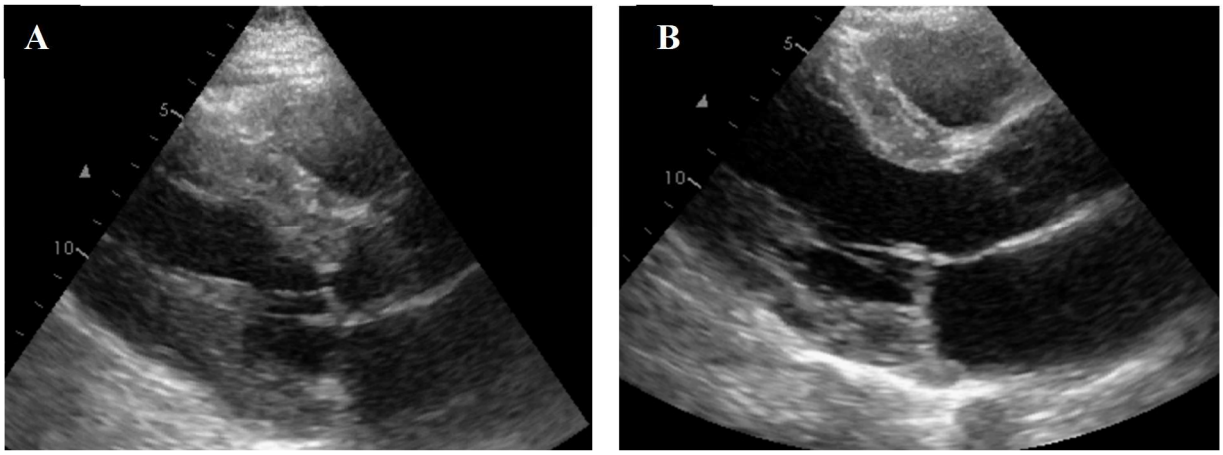

Fig. 2. Intraoperative TEE images before (A) and after (B) procedure, elimination of obstruction on the LVOT by excision of the fibro-muscular band and resection of secondary (pathological) chordae.

In patients with LVOT obstruction accompanied by mid-ventricular obstruction due to hypertrophied PM or muscular bundles, an additional small resection was made at the base of the PM. After removal of the cardiac muscle (myectomy), an intervention on the subvalvular mitral apparatus was performed. Fibrous and muscular structures that connect PM with IVS or LV free wall were present practically in all patients with HCM and were limiting the mobility of the PM. Such structures, that can be identified only at the time of surgery, were systematically resected in each of the examined patient for the purpose of improvement of the PM mobility (PM mobilization). Anomalous chordal structures (pathological secondary chordae) or fibrous attachments between the AML and PM were found in the majority of patients with HCM. These structures routinely underwent resection, which increased the area of coaptation of the MV leaflets and prevented the phenomenon of systolic anterior motion (SAM) in the postoperative period. In cases of diastasis between the places of attachment of the primary chordae to the edge of the MV leaflet over 5 mm, this area was plicated.

The medians of the study were calculated according to the reverse Kaplan–Meier method. Comparisons of continuous variables were performed with the Wilcoxon test. Analyses of change for parameters evaluated before surgery and at the most recent evaluation were performed by means of the McNemar change test and sign test, for binary and continuous variables, respectively. All reported P-values are two-sided. SPSS statistical software (SPSS, Chicago, IL, USA) and MS Excel (Microsoft, Redmond, WA, USA) were used for the calculations.

Results and discussion. In this cohort study, the age of the patients ranged from 7 months to 78 years old (mean 50.1±14.7, median – 54 years). Among them, 12 patients were younger than 18 years old, and eight patients <12 years old. Out of 250 patients included to this study, 93 (37.2%) were in NYHA III-IV functional class at the moment of surgery.

The average cross clamp time accounted 80±10.3 minutes. Septal myectomy was accompanied by AML plication in 146 (58.4%) and MV replacement in 3 (1.2%) out of 250 patients involved in the study. MV replacement was performed in patient with degenerative changes of the leaflets due to severe mitral regurgitation (MR) according to TEE data, as well as occurrence of the acute phase of infective endocarditis in late post-operative period. Other procedures that accompanied septal myectomy, including manipulations on the subvalvular apparatus, are listed in table 2.

Out of 250 patients studied, four (1.6%) underwent implantation of a cardioverter defibrillator (ICD) in the postoperative period to prevent SCD, while 10 (4%) patients underwent pacemaker implantation due to complete AV block. The average length of the in-hospital stay was 10±3 days. The follow-up examination was performed at 3 months, 1, 3 and 5 years after surgery.

Reoperations were performed in 2 patients (0.8%) after 15 and 25 months accordingly after septal myectomy and involved MV replacement due to infective endocarditis.

Table 2

Surgical procedures that accompanied septal myectomy in 250 studied patients

Coronary artery bypass grafting, n (%)	24 (9.6)
Mitral valve replacement, n (%)	3 (1.2%)
AML plication, n (%)	146 (58.4%)
TV annuloplasty, n (%)	5 (2)
AVR, n (%)	6 (5)
ICD implantation, n (%)	4 (1.6)
Robiscek procedure	1 (0.4)
MV subvalvular apparatus	
Resection of the secondary(pathological) chordal attachments between AML and PM of the LV, n (%)	241 (96.4)
Resection of the anomalous ingrown PM to AML, n (%)	11 (4.4)
Resection of fibro-muscular structures between PM and IVS or LV free wall, n (%)	175 (70)
AML – anterior mitral leaflet; AVR – aortic valve replacement; ICD – implantable cardioverter-defibrillator; IVS – interventricular septum; LV – left ventricle; MV – mitral valve; PM – papillary muscle; TV – tricuspid valve	

Out of 250 patients studied, 4 (1.6%) died in the early post-operative period. In total, one case of death associated with chronic respiratory failure in a 65-year-old patient 11 months after surgery and one case of a SCD in a 20-year-old patient 13 months after correction were recorded during follow-up (table 3).

Table 3

Main cardiovascular events after septal myectomy in 250 studied patients

Early (≤30 days after myectomy), n (%)	
Mortality	4 (1.6)
Pacemaker implantation	6 (2.4)
Left bundle branch block	7 (2.8)
Late (≥30 days after myectomy), n (%)	
Pacemaker implantation	4 (1.6)
ICD implantation	4 (1.6)
MV repair	0
MV replacement	2 (0.8)
Cardiovascular death	0
Sudden cardiac death	1 (0.4)
Acute cerebrovascular event (ischemic stroke)	0
Respiratory failure	1 (0.4)
ICD – implantable cardioverter-defibrillator; MV – mitral valve	

The following clinical and echocardiographic evaluation of the patients` condition was performed at the base of our Institute. The SPG on the LVOT was assessed before and after surgical intervention. According to the data obtained, the SPG decreased from 92.8±30.7 mmHg (range 50-235 mmHg) before the surgery to 19.3±8.7 mmHg after correction ($p < 0.001$). 17 patients (6.8%) had residual (≥30 mmHg) SPG on the LVOT at rest or on exertion. Out of 250 patients studied, 44 (17.6%) had residual SPG ≥25 mmHg. Data on NYHA functional class before and after surgery were evaluated in each of the patients involved in the study. Out of 250 patients, 93 (37.2%) of whom were in NYHA functional class III-IV prior to surgery, 154 (61.6%) improved their functional class to I-II at the last evaluation ($p < 0.001$). In addition, there was performed the assessment of MR by echocardiographic examination in patients before and after surgery and distributed on a scale from 0 to 4 (0 – MR is absent, 1 – mild MR, 2 – moderate MR, 3 – moderate-to-severe MR, 4 – severe MR). According to the results of transthoracic echocardiography done after surgery, patients with grade 3 and 4 MR were not identified. 25 (10%) patients with a 2 (moderate) degree of MR were observed, whereas before surgery, the number of patients who had moderate or severe MR was 182 (72.8%) out of 250 individuals ($p < 0.001$).

Among the group of patients included in the study, 16 (6.4%) patients had previously undergone ASA, which proved to be ineffective, and therefore, due to high residual SPG, patients were shown to have surgery. In the post-operative period, all 16 patients (100%) had a satisfactory clinical result of correction – SPG on the LVOT in each of them was <25 mmHg.

The mandatory and the most important stage of the study was SCD risk stratification at 5-year period. Given the exclusion criteria that make it impossible to calculate the risk, out of 250 patients enrolled in the study, the risk of SCD was calculated in 235 individuals (95.2%). Out of 235 patients, 131 (55.7%)

were at low risk, 77 (32.8%) were at moderate risk, 27 (11.5%) were at high risk. In the high-risk group, the average percentage of SCD risk before surgery was 8.43%, while after correction the indicator was 3.78% ($p < 0.002\%$).

The guidelines of the American College of Cardiologists (ACC)/American Heart Association (AHA) and European Society of Cardiology (ESC) have recognized surgical septal myectomy as the gold standard and the primary method of treatment for patients with obstructive HCM.

Up to date, one of the largest series of patients who have undergone septal myectomy is registered in the Cleveland Clinic [2]. This study of a series of 699 patients operated from January 1997 to December 2007 showed the excellent efficacy and safety of the procedure with continuous improvement in symptoms. The mean preoperative maximum LV thickness was 2.2±0.5 cm compared to 1.7±0.5 cm after surgery. The mean preoperative SPG at rest and the peak SPG were 61 and 103 mmHg respectively, in contrast to the average peak gradient of 32 mmHg after surgery. No 30-day mortality was observed, and pacemaker implantation was required only by 7% of patients. In their population, 96% of patients remained asymptomatic or minimally symptomatic (81% NYHA class I and 15% NYHA class II) for an average follow-up of 6.2 years, and freedom from reoperation was 97%.

A critical factor is that HCM still remains to be a complex pathology and therefore requires multistage correction. In order not only to reduce the risk of SCD, but also to provide the patient with an adequate quality of life that will not differ from the quality of life of healthy people, the disappearance of symptoms of heart failure and improve well-being, we have to perform all mandatory stages of correction: extended septal myectomy, resection of secondary (pathological) chordae of the AML, mobilization of the PM and plication of the AML.

Our study has shown that by itself, the myectomy procedure can reduce the risk of SCD in patients with obstructive HCM. This view is shared by Schaff and colleagues [13], who in their work reported that the survival of patients after septal myectomy was higher than the survival of non-operated patients, and this better result was partly due to greater freedom from SCD.

Despite such advances, the issue of SCD prevention remains open. Does septal myectomy actually reduce SCD risk in patients with obstructive HCM? A recent study by Desai and colleagues [2] describes the risk of SCD in a group of 1809 patients with obstructive HCM and compares the observed rates of life-threatening events with those predicted in two different risk models. In addition, 64% of patients underwent septal myectomy. The authors observed a small correlation between the calculated risk score and the actual rates of SCD. In the group of patients who were predicted to be at high risk (9%) of developing SCD or ICD discharge, the 5-year event rate was 4.8%. In addition, life-threatening events were similar among the 3 categories of SCD risk, and after 5 years of follow-up, approximately two-thirds of the events occurred in patients previously classified as low-risk, calculated using the ESC SCD risk calculator.

Standard risk assessment according to the guidelines of the American Heart Association and the American College of Cardiology also had low predictive value, since 65% of events after 5 years occurred in patients without risk factors.

Thus, it is not surprising that the risk models developed for the heterogeneous population of patients with HCM cannot be applied to patients after myectomy, and there are several possible explanations for this. The ESC risk calculator includes SPG, left atrial size, and maximum LV wall thickness in addition to other clinical variables. It is expected that the risk score calculated for the patient with obstruction will change after the gradient on LVOT is relieved.

In addition, the follow-up of patients after myectomy confirms that gradient relief is associated with both a decrease in left atrial size and LV mass [11, 12, 13]. Thus, it is expected that the calculated risk of SCD for an individual patient will change after septal myectomy. Therefore, the question remains: how can one predict the risk of SCD in already operated patients? And how to protect operated patients from life-threatening events?

Conclusion

HCM is a complex pathology which contains several pathophysiological mechanisms that lead to heart failure and high risk of SCD. Multi-stage correction such as extended myectomy, resection of anomalous chordal structures of the MV, mobilization of the PM and plication of the AML allows to influence all links of pathological manifestation of the disease. Surgical septal myectomy not only effectively reduces SPG on the LVOT, decreases the degree of MR and improves the patient's functional class, but also significantly reduces the risk of SCD in patients with obstructive HCM.

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Реферати

РЕЗУЛЬТАТИ ХІРУРГІЧНОГО ЛІКУВАННЯ ПАЦІЄНТІВ З ОБСТРУКТИВНОЮ ФОРМОЮ ГІПЕРТРОФІЧНОЇ КАРДІОМІОПАТІЇ ЯК ФАКТОРУ РИЗИКУ РАПТОВОЇ СЕРЦЕВОЇ СМЕРТІ

Руденко К.В., Лазоришинець В.В., Трембовецька О.М. Невмержицька Л.О., Трегубова М.О., Данченко П.А.

Дослідження включає 250 послідовних симптоматичних пацієнтів з обструктивною формою гіпертрофічної кардіоміопатії (ГКМП), яким було виконано хірургічну розширену міектомію, резекцію аномальних хордальних структур, мобілізацію папілярних м'язів та плікацію передньої стулки мітрального клапана. Мета роботи – провести аналіз ефективності даної методики, а також вивчити безпосередні результати хірургічної корекції у пацієнтів з обструктивною ГКМП. Результати роботи показали статистично значуще зниження систолічного градієнта тиску на вихідному тракті лівого шлуночка, зменшення ступеня мітральної регургітації та покращення функціонального класу NYHA. У 235 пацієнтів проведено стратифікацію ризику раптової серцевої смерті (РСС). Результати дослідження показали, що проведення багатоетапної корекції дозволяє вплинути на всі ланки патологічного прояву даного захворювання, проте постають питання, як спрогнозувати ризик виникнення РСС у вже прооперованих пацієнтів і як захистити їх від життєзагрозливих подій?

Ключові слова: гіпертрофічна кардіоміопатія, розширена септальна міектомія, хірургічна корекція, раптова серцева смерть.

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РЕЗУЛЬТАТЫ ХИРУРГИЧЕСКОГО ЛЕЧЕНИЯ ПАЦИЕНТОВ С ОБСТРУКТИВНОЙ ФОРМОЙ ГИПЕРТРОФИЧЕСКОЙ КАРДИОМИОПАТИИ КАК ФАКТОРА РИСКА ВНЕЗАПНОЙ СЕРДЕЧНОЙ СМЕРТИ

Руденко К.В., Лазоришинец В.В., Трембовецкая Е.М., Невмержицкая Л.А., Трегубова М.А., Данченко П.А.

Исследование включает 250 последовательных симптоматических пациентов с обструктивной формой гипертрофической кардиомиопатии (ГКМП), которым была выполнена хирургическая расширенная миэктомия, резекция аномальных хордальных структур, мобилизация папиллярных мышц и пликация передней створки митрального клапана. Цель работы – провести анализ эффективности данной методики, а также изучить непосредственные результаты хирургической коррекции у пациентов с обструктивной ГКМП. Результаты работы показали статистически значимое снижение систолического градиента давления на выходном тракте левого желудочка, уменьшение степени митральной регургитации и улучшение функционального класса NYHA. У 235 пациентов проведено стратификацию риска внезапной сердечной смерти (ВСС). Результаты исследования показали, что проведение многоэтапной коррекции позволяет повлиять на все звенья патологического проявления данного заболевания, однако возникают вопросы, как спрогнозировать риск возникновения ВСС у уже прооперированных пациентов и как защитить их от жизнеугрожающих событий?

Ключевые слова: гипертрофическая кардиомиопатия, расширенная септальная миэктомия, хирургическая коррекция, внезапная сердечная смерть

Рецензент Старченко І.І.