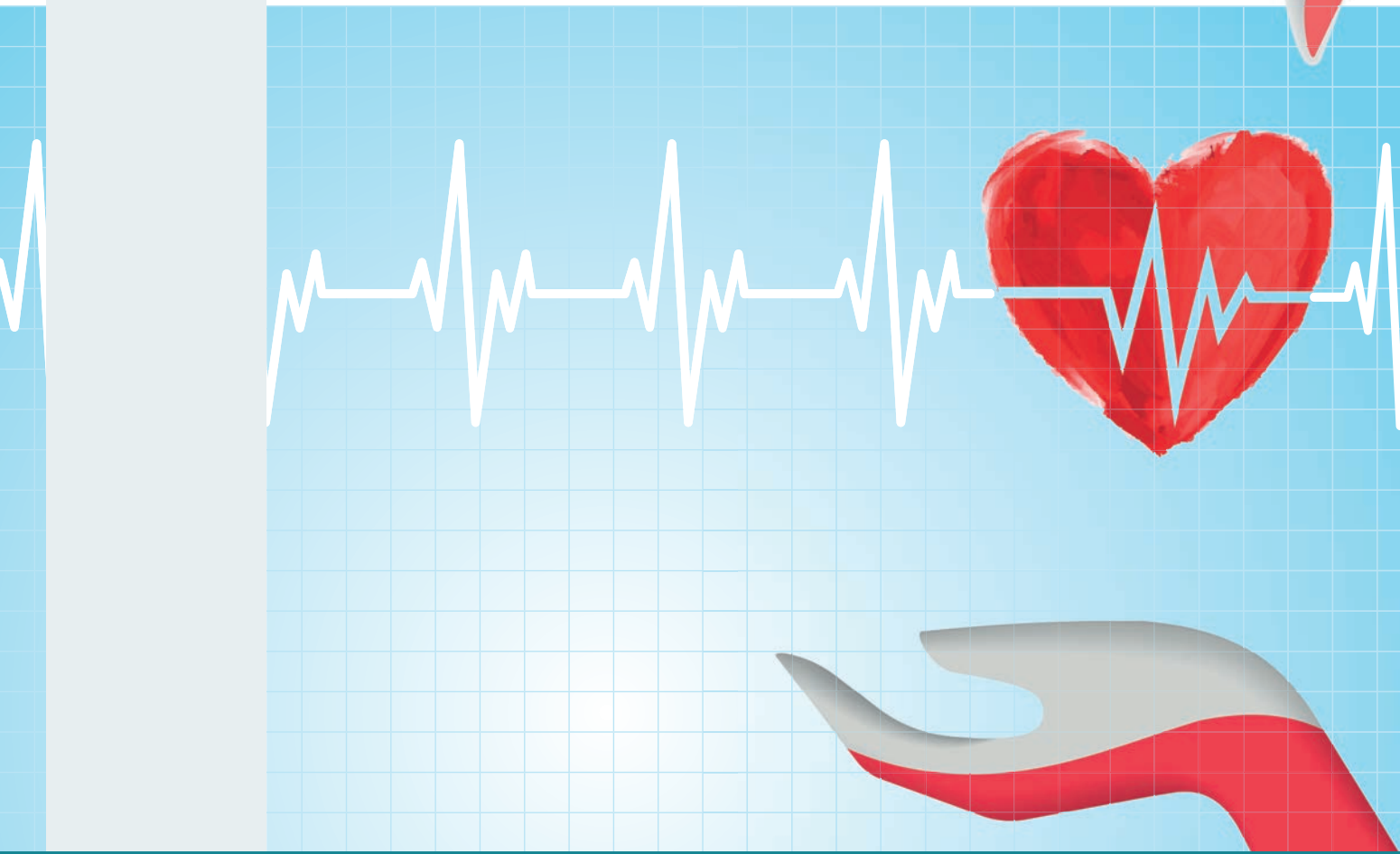
ISSN 2782-4284 (Print)
ISSN 2782-4233 (Online)

VOLUME 3 ISSUE 3 2023

Cardiac Arrhythmias

INTERNATIONAL PEER-REVIEW MEDICAL JOURNAL

https://journals.eco-vector.com/cardar



ЭКО • ВЕКТОР

FOUNDERS

- North-Western State Medical University named after I.I. Mechnikov
- Eco-Vector

PUBLISHER

Eco-Vector
Address:
3A Aptekarskiy lane, office 1N,
Saint Petersburg, 191186, Russia
E-mail: info@eco-vector.com
WEB: https://eco-vector.com
Phone: +7(812)6488367

Federal Supervisory Service on Mass Media, Information Technologies and Mass Communication (Roskomnadzor)
ПИ № ФС77-79865
Published 4 times a year

EDITORIAL

Address:
41 Kirochnaya street,
Saint Petersburg, 191015, Russia
Phone: +7(812)303-50-00
E-mail: ca@eco-vector.com

ADVERTISE

Adv. department
Phone: +7 (495) 308 83 89

OPEN ACCESS

Immediate Open Access is mandatory for all published articles.

SUBSCRIPTION

To the printed version:
Joint catalog "Press of Russia"
on the website https://www.pressa-rf.ru
Index for half yearly subscription – 85697
Index for yearly subscription – 85698
To the electronic version:
https://journals.eco-vector.com
https://elibrary.ru

16+

ISSN 2782-4284 (Print)
ISSN 2782-4233 (Online)

CARDIAC ARRHYTHMIAS

Volume 3 | Issue 3 | 2023

INTERNATIONAL PEER-REVIEW MEDICAL JOURNAL

Published under the supervision of Eurasian Arrhythmology Association

ECO • VECTOR

УЧРЕДИТЕЛИ

- ООО «Эко-Вектор»
- ФГБОУ ВО СЗГМУ им. И.И. Мечникова Минздрава России

ИЗДАТЕЛЬ

ООО «Эко-Вектор»
Адрес: 191186, г. Санкт-Петербург, Аптекарский переулок, д. 3, литера А, помещение 1Н
E-mail: info@eco-vector.com
WEB: https://eco-vector.com
тел.: +7(812)648-83-67

Журнал зарегистрирован Федеральной службой по надзору в сфере массовых коммуникаций, связи и охраны культурного наследия, свидетельство о регистрации СМИ ПИ № ФС77-79865 от 18.12.2020

Выходит 4 раза в год

РЕДАКЦИЯ

191015, Санкт-Петербург, ул. Кирочная, д. 41
Тел.: +7(812)303-50-00
Факс: +7(812)303-50-35
E-mail: ca@eco-vector.com

ПОДПИСКА

На печатную версию журнала: Объединенный каталог «Пресса России» https://www.pressa-rf.ru. Подписной индекс на полугодие — 85697, на год — 85698.
На электронную версию журнала: https://journals.eco-vector.com; eLibrary.ru

OPEN ACCESS

В электронном виде журнал распространяется бесплатно — в режиме немедленного открытого доступа

РЕКЛАМА

Отдел размещения рекламы и репринтов
Тел.: +7 (495) 308 83 89
E-mail: adv@eco-vector.com

Оригинал-макет изготовлен ООО «Эко-Вектор».
Редактор: *И.Л. Уразовская*
Редактор переводческих проектов: *А.А. Богачев*

Формат 60 × 90$^{1}/_{8}$. Печать офсетная.
Усл. печ. л. 7,75. Тираж 200 экз. Цена свободная

Отпечатано в ООО «Типография Экспресс В2В». 191180, Санкт-Петербург, наб. реки Фонтанки, д. 104, лит. А, пом. 3Н, оф. 1.
Тел.: +7(812)646-33-77.
Подписано в печать 27.11.2023.
Заказ 3-10737-lv.
Выход в свет 05.12.2023.

16+

ISSN 2782-4284 (Print)
ISSN 2782-4233 (Online)

CARDIAC ARRHYTHMIAS

Том 3 | Выпуск 3 | 2023

МЕЖДУНАРОДНЫЙ МЕДИЦИНСКИЙ РЕЦЕНЗИРУЕМЫЙ ЖУРНАЛ

Издается под эгидой Евразийской аритмологической ассоциации врачей кардиологов и терапевтов

ЭКО • ВЕКТОР

CONTENTS

СОДЕРЖАНИЕ

DOI: https://doi.org/10.17816/cardar529671

Reseach article

Analysis of the endocardial stage of treatment of tachyarhythmias after open interventions for atrial fibrillation. Experience of one center

Anzhelika S. Postol[1, 2], Georgy N. Antipov[1, 2], Andrei V. Ivanchenko[1], Vitaly V. Lyashenko[1], Dmitriy A. Kalinin[1], Sergey N. Kotov[1], Alexander B. Vygovsky[1], Yuriy A. Schneider[1]

[1] Federal Center for High Medical Technologies Kaliningrad, Kaliningrad, Russia;

[2] Baltic Federal University named after I. Kant, Kaliningrad, Russia

Abstract

AIM: To study EFI parameters and features of recurrent atrial tachyarrhythmias in patients who underwent surgical correction of AF.

MATERIALS AND METHODS: from January 2013 to December 2021, 447 combined interventions were performed to eliminate AF using the labyrinth-3 and left atrial labyrinth techniques with correction of CHD (congenital heart disease) and/or coronary artery disease.

Rhythm disturbances were detected in 57 (12.7%) patients at various follow-up periods. Endovascular interventions were performed in 39 patients. The average follow-up period after the endocardial stage was 34.37 (standard deviation 24.32) months. The median age of patients was 64 (58–67) years, 21 (54%) were men. The patients were divided into 2 groups: group 1 — after the classic biatrial (BA) labyrinth-3 — 23 (59%) patients, group 2 — after the left-atrial variant (LA) labyrinth-3 — 16 (41%) patients.

At the endocardial stage, electrophysiological studies (EFI) were performed to clarify the mechanism of arrhythmia, and ablation eliminated tachyarrhythmia. EFI protocol: revision of the pulmonary veins, determination of the isolation of the posterior wall of the LA assessment of atrial arrhythmia, elimination of arrhythmia, control induction of arrhythmia after ablation. After repeated intervention, patients were observed in the operating clinic every 3 months.

RESULTS: After the endocardial stage, a regular rhythm was determined in 19 (82.6%) patients of the BA group, 13 (92.9%) patients of the LA group ($p = 0.914$). Relapses in the form of AF were noted in 5 patients (4 — group 1 and 1 — group 2) group ($p = 0.306$) All relapses of tachyarrhythmia with an irregular cycle (AF) were detected in patients with AF before the endovascular stage In both groups, there were cases of restoration of conduction in the pulmonary veins — 10 (43.5%) patients after BA ablation and 1 (5.3%) patient after LA ablation. There are no recurrences of atrial arrhythmia after ablation of atrial flutter (arrhythmia with a stable cycle).

CONCLUSION: The endocardial stage is highly effective and demonstrates subsequent freedom from atrial arrhythmia in patients who have tachycardia with a regular cycle after both methods of surgical ablation of AF. Recurrent tachyarrhythmia in the form of AF (irregular cycle) is associated with a low probability of maintaining a regular atrial rhythm after a repeated endocardial procedure, due to the presence of structural and electrophysiological changes in the atrial myocardium.

Keywords: atrial fibrillation; atrial flutter; arrhythmia recurrence; “Maze” procedure; catheter ablation; surgical ablation.

To cite this article

Postol AS, Antipov GN, Ivanchenko AV, Lyashenko VV, Kalinin DA, Kotov SN, Vygovsky AB, Schneider YuA. Analysis of the endocardial stage of treatment of tachyarhythmias after open interventions for atrial fibrillation. Experience of one center. *Cardiac Arrhythmias.* 2023;3(3):5–18. DOI: https://doi.org/10.17816/cardar529671

Received: 03.07.2023 **Accepted:** 14.09.2023 **Published:** 10.11.2023

DOI: https://doi.org/10.17816/cardar529671

Научная статья

Анализ эндокардиального этапа лечения тахиаритмий после открытых вмешательств по поводу фибрилляции предсердий. Опыт одного центра

А.С. Постол[1, 2], Г.Н. Антипов[1, 2], А.В. Иванченко[1], В.В. Ляшенко[1], Д.А. Калинин[1], С.Н. Котов[1], А.Б. Выговский[1], Ю.А. Шнейдер[1]

[1] Федеральный центр высоких медицинских технологий, Калининград, Россия;

[2] Балтийский федеральный университет им. И. Канта, Калининград, Россия

Аннотация

Цель — изучение параметров электрофизиологического исследования и особенностей рецидивов предсердных тахиаритмий пациентов, перенесших хирургическую коррекцию фибрилляции предсердий.

Материалы и методы. С января 2013 по декабрь 2021 года выполнено 447 сочетанных вмешательств устранения фибрилляции предсердий по методикам лабиринт-3 и левопредсердный лабиринт с коррекцией врожденного порока сердца и/или ишемической болезни сердца. У 57 (12,7 %) пациентов в различные сроки наблюдения определены рецидивы нарушения ритма. Выполнены эндоваскулярные вмешательства 39 (8,7 %) пациентам. Средний срок наблюдения после эндокардиального этапа — 34,37 (стандартное отклонение 24,32) мес. Медианный возраст пациентов составил 64 (58–67) года, мужчин 21 (54 %). Пациенты разделены на 2 группы: 1-я группа — после классического биатриального лабиринта-3 — 23 (59 %) пациента, 2-я группа — после левопредсердного варианта лабиринта-3 — 16 (41 %) пациентов. На эндокардиальном этапе выполнены электрофизиологические исследования для уточнения механизма аритмии, аблация, устраняющая тахиаритмию по протоколу: ревизия легочных вен, определение изоляции задней стенки левого предсердия, оценка предсердной аритмии, устранение аритмии, контрольная индукция аритмии после аблации. После повторного вмешательства пациенты каждые 3 мес. наблюдались в оперирующей клинике.

Результаты. После эндокардиального этапа регулярный ритм определяется у 19 (82,6 %) пациентов 1-й группы, 13 (92,9 %) пациентов 2-й группы (p = 0,914). Рецидивы в виде фибрилляции предсердий — у 5 (4 (17,4 %) в 1-й группе и 1 (7,1 %) во 2-й группе) пациентов (p = 0,306). Все рецидивы тахиаритмии с нерегулярным циклом фибрилляции предсердий выявлены у пациентов с ФП перед эндоваскулярным этапом. В обеих группах выявлены случаи восстановления проведения в легочных венах — у 10 (43,5 %) пациентов после биатриальной аблации и 1 (5,3 %) пациента после левопредсердной аблации. Рецидивы предсердной аритмии после аблации трепетания предсердий (аритмии со стабильным циклом) отсутствовали.

Заключение. У пациентов, имеющих после применения обоих методов хирургической аблации фибрилляции предсердий тахикардии с регулярным циклом, эндокардиальный этап высокоэффективен и демонстрирует последующую свободу от предсердной аритмии. Рецидив тахиаритмии в виде фибрилляции предсердий (нерегулярный цикл) ассоциирован с низкой вероятностью удержания регулярного предсердного ритма после повторной эндокардиальной процедуры, что можно объяснить наличием структурных и электрофизиологических изменений в миокарде предсердий.

Ключевые слова: фибрилляция предсердий; трепетание предсердий; рецидив аритмии; хирургическая процедура лабиринт; катетерная аблация; хирургическая аблация.

Как цитировать

Постол А.С., Антипов Г.Н., Иванченко А.В., Ляшенко В.В., Калинин Д.А., Котов С.Н., Выговский А.Б., Шнейдер Ю.А. Анализ эндокардиального этапа лечения тахиаритмий после открытых вмешательств по поводу фибрилляции предсердий. Опыт одного центра // Cardiac Arrhythmias. 2023. Т. 3, № 3. С. 5–18. DOI: https://doi.org/10.17816/cardar529671

Рукопись получена: 03.07.2023 **Рукопись одобрена:** 14.09.2023 **Опубликована:** 10.11.2023

INTRODUCTION

Although atrial fibrillation (AF) is not a life-threatening arrhythmia, the negative components of this atrial arrhythmia, namely, embolic complications, structural heart pathologies, and high all-cause mortality, can hardly be overestimated [1]. Current meta-analyses indicate that biatrial ablation promotes long-term freedom from recurrent AF and may be indicated in patients with long-term persistent AF [2–4]. In addition to restoring and maintaining a regular atrial rhythm, surgical ablation demonstrates to improve the psychological and physical components of the quality of life of patients compared with other methods for AF ablation [5]. Despite the nearly radical elimination of the main mechanisms supporting AF through open surgery using the classical maze III procedure, some patients are diagnosed with clinically significant relapses of rhythm disorders that require additional catheter procedures [4, 6–12]. The concept of a "hybrid approach to AF treatment", which emerged in the last decade, implies the possibility of performing the next endocardial stage (or stages) following surgical interventions to eliminate AF or implant devices for rhythm control [13–16]. During the endocardial stage, arrhythmia can be verified, and the presence of scar fields in the atrial structure and parameters of low-amplitude segments can be determined [17]. These zones have significantly different myocardial structures, extent, and localization and contribute to the probability of maintaining a regular atrial rhythm, and restoring the systolic contribution of the atria to myocardial kinetics. Accordingly, this paper presents an analysis of long-term results based on the maintenance of regular atrial rhythm after two methods of the surgical correction of AF, and an assessment of the efficiency of the subsequent endocardial ablation stage.

This study aimed to analyze the incidence of relapses and results of the treatment of atrial arrhythmias in patients who underwent various types of surgical ablation of AF during combined cardiac interventions.

MATERIALS AND METHODS OF RESEARCH

The study enrolled patients who underwent surgery at the Federal Center for High Medical Technologies (FCHMT) in Kaliningrad between January 2013 and December 2021. A total of 447 combined interventions were performed to eliminate AF using maze III (217) and left atrial (LA) maze (230) methods and correct other cardiac pathologies, such as acquired heart disease (AHD) and/or ischemic heart disease (IHD).

The indications for surgical and endocardial intervention include the presence of AF or its relapse (if referred to the endocardial stage) > 3 months after surgery, concomitant cardiac pathology such as AHD or lesions of the coronary arteries in IHD, relapses of various atrial tachyarrhythmias, and ineffectiveness of antiarrhythmic therapy based on Heart Rhythm Society/European Heart Rhythm Association/ European Cardiac Arrhythmia Society guidelines [1].

Initially, when referred for surgical and subsequently endocardial correction of tachyarrhythmias, all patients had comparable demographic and clinical characteristics (Table 1).

This retrospective, uncontrolled study with an interrupted time series of two groups depending on the surgical treatment option for AF was assessed and approved by the members of the ethics committee of the FCHMT (Protocol No. 4 of 11/01/2021).

In 57 (12.7%) patients, tachyarrhythmias relapsed at various times after surgery. Only the following patients were enrolled for the endocardial ablation stage:

1) Patients with maintained regular atrial rhythm after the surgical correction of AF and subsequently diagnosed with relapse of atrial tachyarrhythmia at the outpatient follow-up.

2) Patients without persistent sinus rhythm after the surgical correction of AF despite therapy aimed at restoring and maintaining the rhythm (twice electrical cardioversion [ECV], correction of antiarrhythmic therapy, and electrolyte and metabolic disorders). Such patients were referred to the endocardial ablation stage > 3 months after the surgical correction of AF.

Of the 57 patients, 39 (68.4%) received repeated interventions, or 8.7% of the combined open interventions were performed. The average follow-up period after the endocardial stage of treatment was 34.37 (standard deviation, 24.32) months. The median age of the patients was 64 (58–67) years. The study enrolled 21 (54%) men and 17 (46%) women. The patients were distributed into two groups: group 1 underwent the classic biatrial (BA) maze III surgery (n = 23, 59%), and group 2 underwent the LA version of maze III (n = 16, 41%).

During the follow-up period, every 3 months after re-intervention, electrocardiographic (ECG) rhythm recording, Holter ECG monitoring, echocardiography (EchoCG), and programming of the pacemaker with analysis of atrial electrograms were performed. The presence of implanted pacemakers was considered a positive factor for detailed verification of the atrial rhythm. The study aimed to assess electrophysiological heart test (EPT) parameters and the characteristics of recurrent atrial tachyarrhythmias in patients who had a history of surgical correction of AF and who were heterogeneous according to the primary selection criteria. Relapses of atrial arrhythmias were differentiated by the presence of regular and irregular cycles, endocardial

Table 1. Clinical characteristics of patients who underwent surgery
Таблица 1. Клиническая характеристика пациентов, перенесших хирургическое вмешательство

Parameters	Group 1 (*n* = 23)	Group 2 (*n* = 16)	*p*
Age, years, *Me*	63 (45–70)	63 (43–73)	0.810
Sex, F/M	9/14 (39/61)	12/4 (75/25)	0.027
Duration of AF before surgery, months (*Me*)	60 (6–240)	48 (6–156)	0.746
AF type:			
Paroxysmal, *n* (%)	2 (8.7)	1 (6.2)	0.779
Persistent, *n* (%)	21 (91.3)	15 (93.8)	0.779
LA volume before the surgical stage, mm^3 (*Me*)	121.2 (80–180)	148.7 (100–350)	0.935
LA volume before the endovascular stage, mm^3 (*Me*)	118.1 (70–138)	111.5 (75–124)	0.140
CABG, *n* (%)	11 (47.8)	8 (50.0)	0.322
Mitral and tricuspid valve repair, *n* (%)	3 (13.0)	2 (12.5)	0.240
MV prosthesis, *n* (%)	5 (8.7)	3 (18.7)	0.064
Mitral valve repair, *n* (%)	9 (39.1)	8 (50.0)	0.401
AV prosthesis, *n* (%)	4 (17.4)	2 (12.5)	0.275
De-Vega repair of the TV, *n* (%)	10 (43.3)	9 (56.3)	0.799
LVEF% (%) before the surgical stage (initial)	47.1 (22.0–61.0)	48.2 (30.0–60.0)	0.143
LVEF% (%) before the endocardial stage,	51 (38.0–60.0)	53 (40–62)	0.411
CHD, *n* (%)	3 (13.0)	1 (16.0)	0.410
AHD, *n* (%)	13 (56.5)	8 (50.0)	0.420
Beta blocker therapy, *n* (%)	10 (50.0)	7 (43.7)	0.398
Diuretic therapy, *n* (%)	4 (17.4)	3 (18.7)	0.440
Anticoagulant therapy, *n* (%)	19 (82.7)	12 (75.0)	0.414

Note: AF — atrial fibrillation; AHD — acquired heart defect; AV — aortic valve; BA — biatrial maze; CABG — coronary artery bypass grafting; CHD — congenital heart defect; EF — ejection fraction; LA — left atrial maze; LA — left atrium; MV — mitral valve; TV — tricuspid valve.

Примечание: ФП — фибрилляция предсердий; ФВ — фракция выброса; ЛП — левое предсердие; АКШ — аортокоронарное шунтирование; МК — митральный клапан; ТК — трикуспидальный клапан; АК — аортальный клапан; БА — биатриальный лабиринт; ЛП — левопредсердный лабиринт; ВПС — врожденный порок сердца; ППС — приобретенный порок сердца.

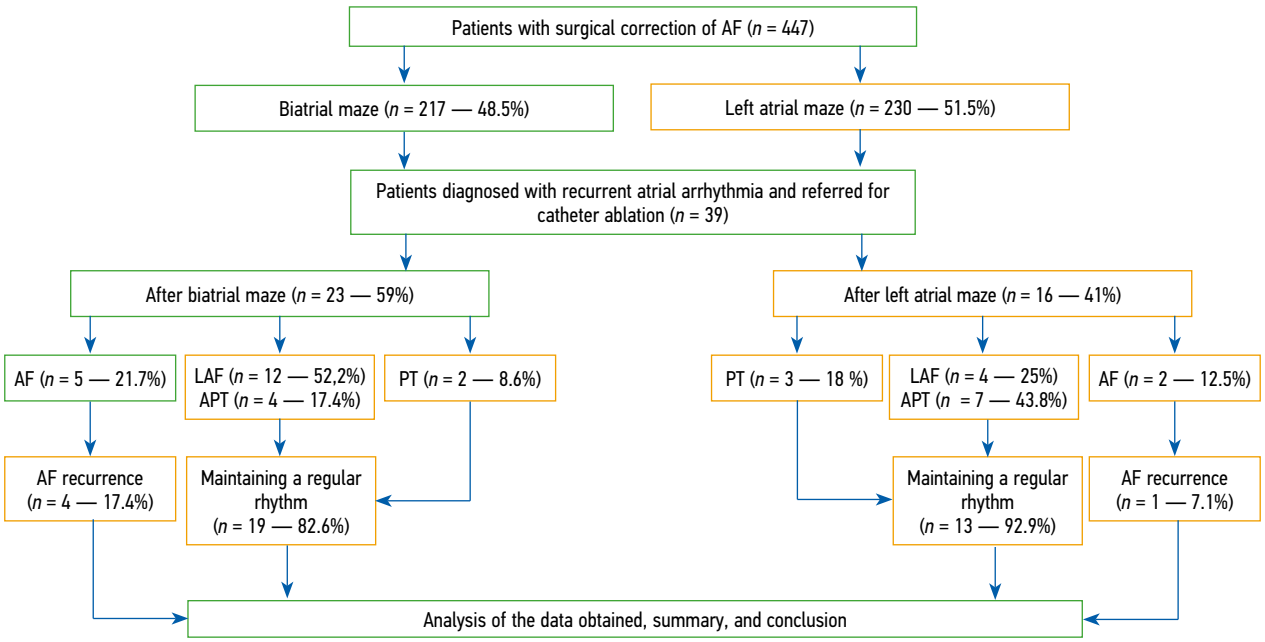


Fig. 1. Design diagram of the completed study
Рис. 1. Дизайн-схема выполненного исследования. ФП — фибрилляция предсердий; РЧА — радиочастотная аблация; ПТ — пароксизмальная тахикардия; ППТ — предсердная пароксизмальная тахикардия

correction of tachyarrhythmias was performed, and rhythm maintenance was assessed.

Statistical processing

The results were statistically analyzed using IBM Statistics for Windows version 21.0 (IBM Corp., Armonk, NY, USA). Normally distributed indicators are presented as the average value for the sample and its standard deviation ($\overline{X} \pm sd$), whereas non-normally distributed indicators are presented as medians and interquartile ranges, *Me* (min–max). When scores were normally distributed, paired Student's *t*-tests for related and unrelated samples were used to test the null hypothesis. When the distribution differs from the normal, the χ^2 (Chi-square) test was used to assess the statistically significant difference between nominative indicators. To assess the quantitative indicators of two unrelated samples, the Mann — Whitney *U*-test was used.

Subgroup characteristics for continuous measures are presented as mean ± standard deviation. For qualitative indicators, numerical data and percentages are given. Differences in indicators between groups were defined as statistically significant at $p < 0.05$.

Endovascular intervention

Catheter intervention was performed using the Carto (Biosense Webster, USA) and Ensite (Abbott, USA) navigation systems. The diagnostic electrodes used were the 10-pole electrode for coronary sinus catheterization (Biosense Webster) and the 10-pole Lasso electrode (Biosense Webster). For mapping and ablation, the ablation-mapping irrigated SmartTouch (Biosense Webster) and CoolFlex (Abbott) were used. The ablation parameters were 30–45 W and exposure duration of 30–60 s. The irrigation rates were 17–28 and 25–35 mL/min for CoolFlex and SmartTouch, respectively.

After the catheterization of the coronary sinus, to assess the type of atrial arrhythmia, regularity of the tachyarrhythmia cycle, its duration, and spread of the arrhythmia activation front were assessed. Then, the presence of conduction in the pulmonary veins (PVs), consistency of the isolation of the LA posterior wall, and the intensity and number of low-amplitude zones in the atria were assessed. An amplitude of the recorded signal of ⩽0.2 mV from the electrode along the coronary sinus was considered low. When an arrhythmia with a regular cycle of atrial flutter was detected, differential diagnostics of the flutter substrate cavity (right atrial or LA flutter) was performed. The type of flutter was clarified according to the criteria of analyzing the activation front and determining the involvement of the treatment electrode location relative to the arrhythmia cycle. If LA flutter was detected, subsequent EPT and ablation techniques were similar to that for AF. The interatrial septum was punctured twice using Preface Multipurpose introducers (Cordis, USA) under X-ray control. Then, three-dimensional endocardial reconstruction of the left or right atrium, amplitude mapping to identify scar areas in the left and right atria (Fig. 2), and activation mapping with a window of interest 10–20 ms shorter than the tachycardia cycle was performed. In the case of atrial flutter, ablation was performed along the identified critical conduction zones with the creation and mandatory monitoring of the presence of a bidirectional conduction block (at least 140 ms). The criteria for the formation of a conduction block during atrial flutter include an episode of the formation of "double" spikes and a sharp prolongation of signal transmission according to the endogram data on the treatment electrode.

In the presence of conduction breakthroughs in the PVs or posterior wall of the left atrium, radiofrequency (RF) re-isolation was performed to monitor the absence of conduction (monitoring during high-frequency [HF] influences and again at the end of the procedure for tachyarrhythmias and after ECV).

The ablation scheme for persistent tachyarrhythmia with an irregular cycle included a mandatory anteroseptal line from the mitral valve to the superior right PV, at the base of the ligated or resected LA appendage and along the coronary sinus, and the interatrial septum on the right and left. An intercaval line and isolation of the superior vena cava were performed if a right atrial role in maintaining rhythm disorders was assumed and right atrial arrhythmia with a regular cycle was excluded (with the analysis of the arrhythmia cycle, its duration, and propagation of the arrhythmia activation front). When the AF transitioned to atrial flutter or atrial extrasystole, ablation was performed according to the criteria of the newly recorded arrhythmia (cycle regularity and duration and analysis of the activation front based on recordings from the coronary sinus) and ablation of areas critical for tachycardia after the clarification of the specified parameters. For focal atrial tachycardias, mapping was performed according to the protocol for

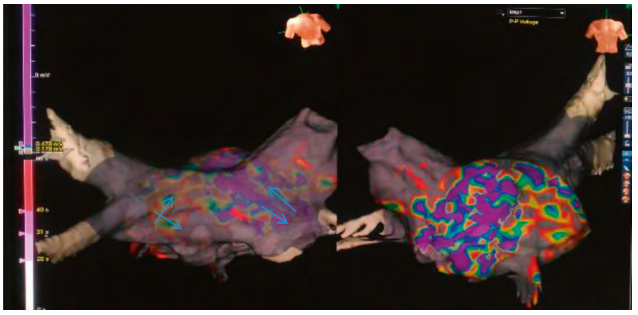


Fig. 2. Typical amplitude map of a patient after labyrinth-3 surgery. The arrows indicate zones of absence of electrical activity in all pulmonary veins and the posterior wall of the left atrium
Рис. 2. Типичная амплитудная карта пациента после операции лабиринт-3. Стрелками указаны зоны отсутствия электрической активности всех легочных вен и задней стенки левого предсердия

Table 2. Type of tachyarrhythmia according to electrophysiological studies
Таблица 2. Вид тахиаритмии по данным электрофизиологического исследования

Parameters	Group 1 (*n* = 23)	Group 2 (*n* = 16)	*p*
AF	5 (21.7)	2 (12.5)	0.460
Left atrial AFl	12 (52.2)	4 (25)	0.090
Right atrial AFl	4 (17.4)	7 (43.8)	0.072
AT	2 (8.6)	3 (18.7)	0.356

Note: AF — atrial fibrillation; AFl — atrial fluttering; AT — atrial tachycardia; BA — biatrial; LA — left atrial.

Примечание: БА — биатриальный; ЛП — левопредсердный; ФП — фибрилляция предсердий; ТП — трепетание предсердий; ПТ — предсердная тахикардия.

searching for the earliest activation area from the reference electrode. The criteria for atrial tachycardia included tachycardia incidence different from flutter, presence of an unstable cycle (warming up and cooling down of tachycardia), impossibility of constructing an activation map owing to the absence of a macro re-entry tachycardia mechanism, and eliminating tachycardia by determining the earliest activation zone from the treatment electrode. If AF persisted and/or the tachyarrhythmia cycle was not organized, ECV was performed after all interventions, with mandatory restoration of sinus rhythm in each patient. After eliminating atrial tachyarrhythmia, in each patient, the consistency of HF influences was also tested. The presence or absence of a conduction block was analyzed by recording signals from the treatment and Lasso electrodes. The absence of spike activity in the electrodes was regarded as the blockade of arrhythmic activity. The consistency of the lines was assessed by the achievement of a bidirectional conduction block (at least 140 ms).

After the analysis of the consistency of the effects through frequent stimulations using a therapeutic electrode and an electrode installed in the coronary sinus, arrhythmia was induced. The stimulation parameters were selected based on the tachyarrhythmia data of each patient, with atrial flutter and stimulation with a tachycardia cycle duration of 10–20–30 ms less than the initial arrhythmia cycle. Frequent and ultra-frequent stimulations (stimulation cycle duration sequentially 300–250–200 ms) were also performed to induce AF. The procedure was completed if, despite the "active" induction of arrhythmia, a regular atrial rhythm was maintained.

RESULTS

Tachyarrhythmia recurrence parameters after two methods of surgical treatment of AF

To determine the recurrence parameters of atrial arrhythmias, the indicators of significant differences in clinical and demographic criteria between groups were analyzed. In the two groups, 9 (39%) and 12 (75%) female patients with recurrent atrial arrhythmias underwent surgery. No sex differences were found among patients who underwent various types of surgical ablation of AF during combined cardiac interventions.

According to the endogram recordings from the coronary sinus, no significant differences in the type of atrial tachyarrhythmias were detected between the two groups. LA flutter was diagnosed in 12 (52.2%) and 4 (25%) patients, right atrial fluttering in 4 (17.5%) and 7 (43.8%) patients, AF in 5 (21.7%) and 2 (12.5%) patients, and atrial tachycardias in 2 (8.6%) and 3 (18.7%) patients, in groups 1 and 2 respectively (Table 2).

The lack of isolation of the LA posterior wall was detected in 6 (26%) patients of group 1 and 4 (25%) of group 2 (p = 0.875). The shortcoming in both groups was the roof at the confluence of the superior left PV; basically, the re-isolation of the posterior wall of the PVs was achieved there. PV re-isolation was also often achieved by performing additional ablations along the posterior wall of the right PVs (Figs. 3 and 4).

Recanalization of conduction in the PVs was identified in 10 (43.5%) patients in group 1 and 1 (5.3%) patient in group 2. In all cases, only segmental ablation was required to eliminate conduction breakthroughs in the PVs. An anterior septal line was made in 8 (34.8%) patients in group 1 and 4 (25%) patients in group 2 (ablation was performed until a bidirectional conduction block of at least 140 ms was achieved; p = 0.400), as well as in the mitral isthmus in 4 (17.4%) patients in group 1 and 4 patients (25.0%) in group 2 (p = 0.563). During resection and successful ligation of the LA appendage in patients with AF, anteroseptal and mitral lines were performed in some cases, excluding the base of the appendage stump, because pronounced rhythmic activity was recorded there. However, after linear influences, no arrhythmia or restoration of sinus rhythm was organized. In these patients, extrapulmonary foci played the leading role in maintaining arrhythmia against progressive cardiosclerosis in both atria and interatrial septum. In the cavotricuspid

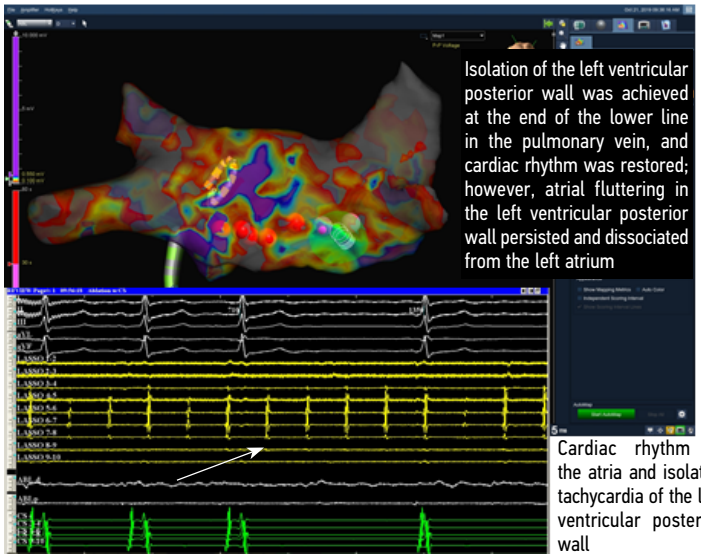


Fig. 3. Amplitude map and recording of the electrocardiogram and endograms of the patient after the labyrinth-3 operation. *Top–down*: amplitude map of the patient, standard electrocardiogram leads, and signals from the multipole circular electrode (yellow) on the posterior wall of the left atrium, where the arrows indicate the activity from the anastomosis on the left, signals from the ablation electrode (white), and signals from the multipole electrode in the coronary sinus (green). Isolation of the posterior wall was achieved, the dissociation of arrhythmic activity corresponded to data from the Lasso catheter, and flutter persists, and sinus rhythm exists along the electrode from the coronary sinus (also the arrowhead is the lower horizontal arrow on the recording from the coronary sinus). The EPT system "Claris" (Abbott, USA) was used. The recording speed was 200 mm/s

Рис. 3. Амплитудная карта и запись электрокардиограммы и эндограмм пациента после операции лабиринт-3. *Сверху вниз*: амплитудная карта пациента, стандартные отведения ЭКГ, сигналы с многополюсного циркулярного электрода (желтые) на задней стенке левого предсердия — стрелками указана активность с соустья слева, сигналы с аблационного электрода (белые), сигналы с многополюсного электрода в коронарном синусе (зеленые). Изоляция задней стенки достигнута, диссоциация аритмической активности — по данным с катетера «Lasso», сохраняется трепетание, при этом по электроду из коронарного синуса — синусовый ритм (также стрелка-указатель — нижняя горизонтальная стрелка на записи с коронарного синуса). ЭФИ-система «Claris» (Abbot, США). Скорость записи 200 мм/с

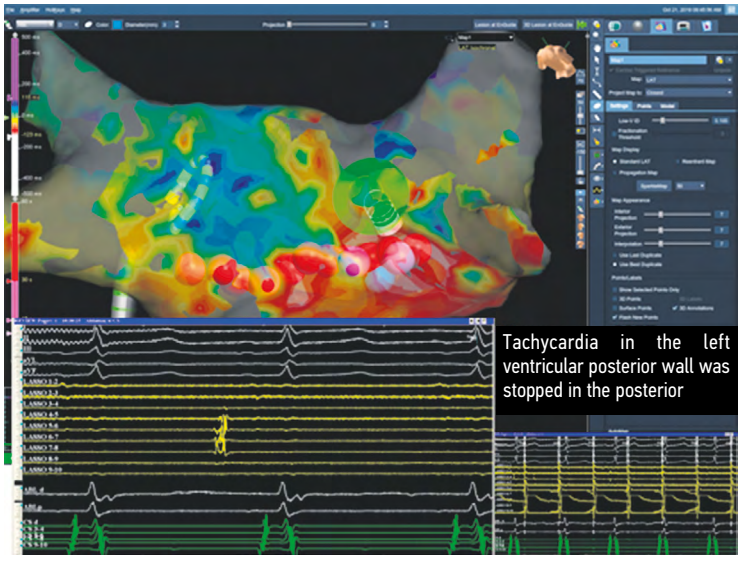


Fig. 4. Relief of tachycardia in the posterior anastomosis on the right. *Top–down*: amplitude map of the patient, standard leads of the electrocardiogram, and signals from the multipole circular electrode (yellow) on the posterior wall of the left atrium. The arrows indicate the absence of activity from the anastomosis on the right, where the treatment electrode is located. White, signals from the ablation electrode; green, signals from the multipole electrode in the coronary sinus. The Claris EPT system (Abbott, USA) was used. The recording speed was 200 mm/s

Рис. 4. Купирование тахикардии в заднем соустье справа. *Сверху вниз*: амплитудная карта пациента, стандартные отведения электрокардиограммы, сигналы с многополюсного циркулярного электрода (желтые) на задней стенке левого предсердия стрелками указано отсутствие активности с соустья справа, там, где располагается лечебный электрод, сигналы с аблационного электрода (белые), сигналы с многополюсного электрода в коронарном синусе (зеленые). ЭФИ-система Claris (Abbot, США). Скорость записи 200 мм/с

region, ablation was needed in 4 patients (17.4%) in group 1 and 7 patients (43.8%) in group 2 (p = 0.091). The intercaval line was made in 2 patients (9.1%) only in the maze III group in cases of "silent" left atrium. Against cicatricial changes when relieving the main rhythm disorder during the ablation procedure, the tachycardia cycle often transformed. This happened in 8 patients (36.4%) and 3 patients (18.8%) of both groups, respectively (p = 0.203). Atrial extrasystoles often occurred after relief, requiring additional interventions. The restoration of sinus rhythm upon the closure of the ablation line was recorded in 15 patients (71.4%) of group 1 and 14 patients (87.5%) of group 2 (p = 0.117; Fig. 5).

Table 3 presents the interventions performed and the arrhythmia parameters. In all patients, after the arrest

Table 3. Performed interventions and arrhythmia parameters
Таблица 3. Выполненные воздействия и параметры аритмий

Parameter	BA group (n = 23)	LA group (n = 16)	p
LA posterior wall isolation, n (%)	6 (26)	4 (25)	0.940
LA roof, n (%)	2 (8.7)	2 (12.5)	0.701
MI, n (%)	4 (17.4)	4 (25)	0.563
CTI, n (%)	4 (17.4)	7 (43.8)	0.091
Breakthrough in the PV, n (%)	10 (43.5)	1 (5.3)	0.02
Anteroseptal line, n (%)	8 (34.8)	4 (25)	0.515
Isolation of the superior vena cava, n (%)	1 (4.3)	1 (6.25)	0.792
ECV relief, n (%)	4 (30.8)	3 (21.4)	0.914
RFA relief, n (%)	15 (71.4)	14 (87.5)	0.117
Low-amplitude EG, n (%)	12 (52.2)	9 (56.3)	0.802
Cycle switching, n (%)	8 (36.4)	3 (18.8)	0.274
Low-signal amplitude based on the recording from the coronary sinus, n (%)	13 (59)	9 (56)	0.228

Note: CTI — cavatricuspid isthmus; ECV — electrical cardioversion; EG — electrogram; LA — left atrium; MI — mitral isthmus; PV — pulmonary veins; RFA — radiofrequency ablation.

Примечание: ЛП — левое предсердие; МИ — митральный истмус; КТИ — каватрикуспидальный истмус; ЛВ — легочные вены; ЭИТ — электроимпульсная терапия; РЧА — радиочастотная аблация; ЭГ — электрограмма.

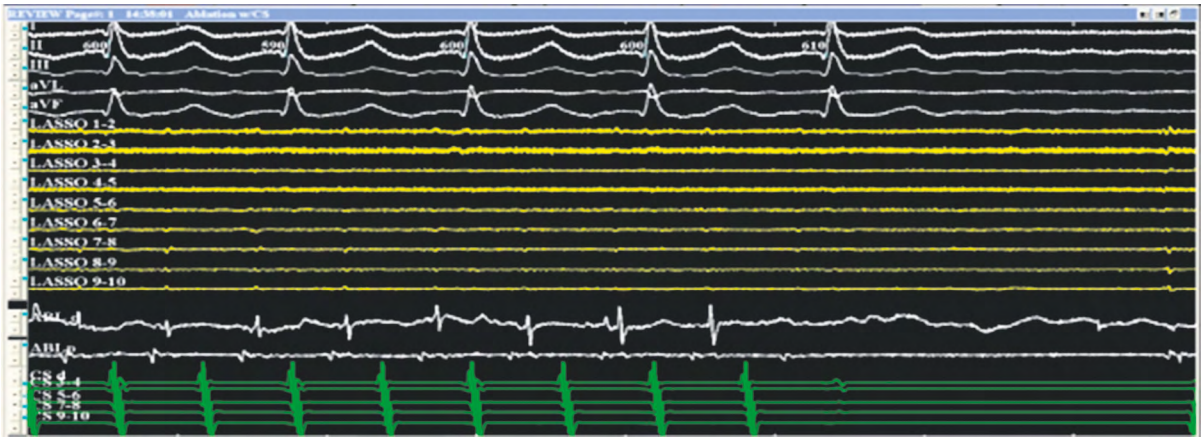


Fig. 5. Fragment of the operation of radiofrequency ablation of septal atrial flutter after the labyrinth-3 operation, arrest of arrhythmia and restoration of sinus rhythm during ablation. *Top–down:* standard electrocardiogram leads, signals from a multipole circular electrode (yellow) on the left atrial posterior wall, signals from an ablation electrode (white), and signals from a multipole electrode in the coronary sinus (green). The EPT system "Claris" (Abbott, USA) was used. The recording speed was 200 mm/s

Рис. 5. Фрагмент операции радиочастотной аблации септального трепетания предсердий после операции лабиринт-3, купирование аритмии и восстановление синусового ритма во время аблации. *Сверху вниз*: стандартные отведения ЭКГ, сигналы с многополюсного циркулярного электрода (желтые) на задней стенке левого предсердия, сигналы с аблационного электрода (белые), сигналы с многополюсного электрода в коронарном синусе (зеленые). ЭФИ система «Claris» (Abbot, США). Скорость записи 200 мм/с

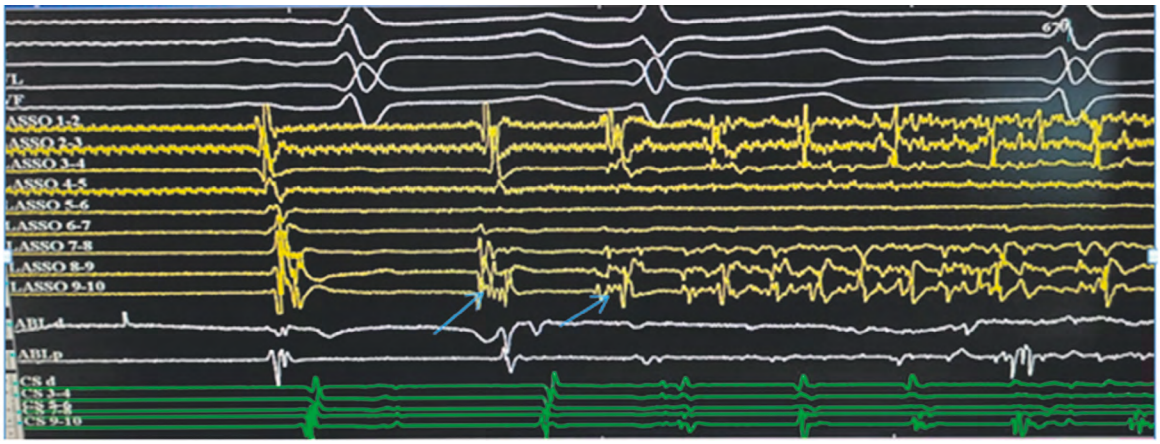


Fig. 6. Re-induction of atrial fibrillation after cardioversion. The arrows indicate the onset of atrial fibrillation through several sinus complexes immediately after cardioversion. *Top–down:* standard electrocardiogram leads, signals from a multipole circular catheter "Lasso" located in the superior vena cava (yellow endograms) which starts from a single ectopy (the earliest signal during the start of an arrhythmia) and transforms into arrhythmic fibrillatory activity (also indicated by an arrow), signals from the ablation electrode (white), and signals from the multipole electrode in the coronary sinus (green). The EPT system "Claris" (Abbott) was used. The recording speed was 200 mm/s

Рис. 6. Повторная индукция фибрилляции предсердий после кардиоверсии. Стрелками указан старт фибрилляции предсердий через несколько синусовых комплексов сразу после проведения кардиоверсии. *Сверху вниз*: стандартные отведения электрокардиограммы, сигналы с многополюсного циркулярного катетера «Lasso» расположенном в верхней полой вене (желтые эндограммы) — запуск с одиночной эктопии (самый ранний сигнал во время запуска аритмии) и трансформация в неритмичную фибрилляторную активность (также указание стрелкой), сигналы с аблационного электрода (белые), сигналы с многополюсного электрода в коронарном синусе (зеленые). ЭФИ-система «Claris» (Abbot). Скорость записи 200 мм/с

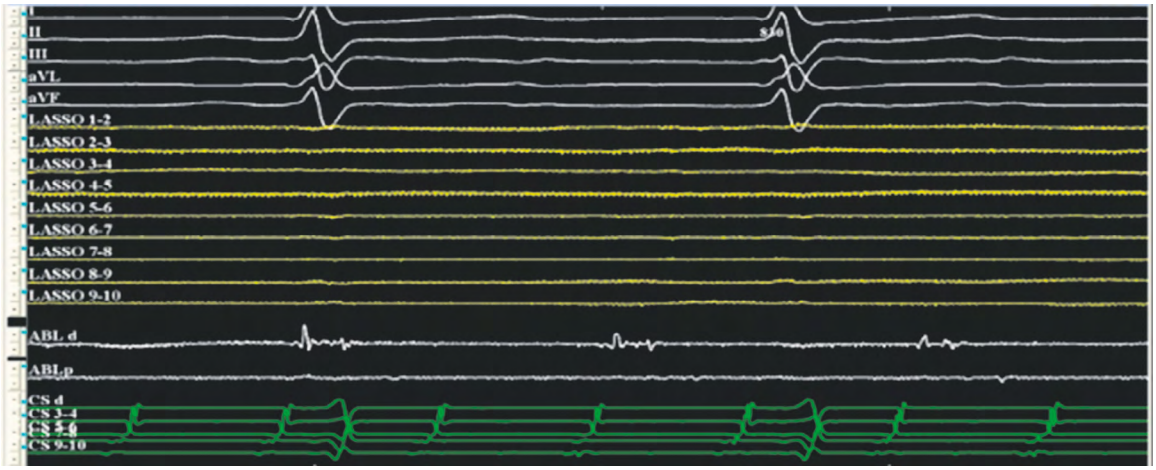


Fig. 7. Atrial flutter in a patient after labyrinth-3 surgery. *Top–down*: standard electrocardiogram leads, signals from a multipole circular electrode on the left atrial posterior wall (yellow), signals from the ablation electrode (white), ablation electrode located on a partially isolated site of the atrial myocardium, and signals from the multipole electrode in the coronary sinus (green). The EPT system "Claris" (Abbott, USA) was used. The recording speed was 200 mm/s

Рис. 7. Трепетание предсердий у пациента после операции лабиринт-3. Стрелками указаны низкоамплитудные фрагментированные сигналы. *Сверху вниз*: стандартные отведения электрокардиограммы, сигналы с многополюсного циркулярного электрода на задней стенке левого предсердия (желтые), сигналы с аблационного электрода (белые). Аблационный электрод расположен на частично изолированном участке миокарда предсердий, сигналы с многополюсного электрода в коронарном синусе (зеленые). ЭФИ-система «Claris» (Abbot, США). Скорость записи 200 мм/с

of arrhythmias during the ablation procedure, repeated inductions did not provoke the appearance of arrhythmias with previously diagnosed parameters in all cases (100%). The consistency of the lines must be monitored on stimulation from the treatment electrode. If not divided into groups, 3 (1–8) linear influences were performed on average on each patient. AF persisted despite all the effects, and ECV was required in 4 (30.8%) patients in group 1 and 3 (21.4%) in group 2 (p = 0.914). Repeated ECVs were performed in three patients because of AF onset (Fig. 6). The amplitude of the signal from the electrode along the coronary sinus was low, i.e., < 0.2 mV, and was detected in 13 patients (59%) in group 1 and 9 (56%) in group 2 (Fig. 7). Such signal amplitude parameters

were attributed to atrial cardiosclerosis and structural remodeling. During this study, the low-amplitude zones in each case were not determined; perhaps this will be conducted in subsequent studies.

Electrophysiological aspects during the electrophysiological study after two options for the surgical treatment of AF

Owing to the presence of massive cicatricial changes in the atria, interventions resulting in the occurrence of cicatricial changes along the coronary sinus, and the absence of the LA appendage, difficulties are noteworthy in choosing a stable reference channel for activation mapping. After constructing an activation map, the simultaneous presence of several "early-late" fields is often diagnosed due to the presence of consistent lines (surgical cut-and-sew correction of arrhythmia). Owing to massive scar changes in the atria and the interventions performed, stimulation was difficult even at 20 mA with a pulse duration of 4 ms. The EPT aspects presented the need for additional control of the treatment electrode location relative to the arrhythmia cycle, and the procedure duration was increased. Ablation after maze III is characterized by the presence of extensive fibrous fields with slow electrophysiological activity up to LA asystole in comparison with the preserved fibrillatory activity in the right atrium and interatrial septum. The classic maze III procedure prevents right atrial arrhythmias in the postoperative period. Such a pattern was not found when we performed ablation after an isolated LA maze.

Patient follow-up after the endocardial stage

The average follow-up period after the endocardial stage of treatment was 34.37 (standard deviation, 24.32) months. A regular atrial rhythm was maintained in 19 (82.6%) and 13 (92.9%) patients in groups 1 and 2, respectively (p = 0.914). AF relapses occurred in 4 (17.4%) patients in group 1 and 1 (7.1%) in group 2.

All cases of AF relapse were recorded in patients with arrhythmias previously diagnosed at the endocardial stage in the form of AF and atrial tachycardia. After RF ablation of atrial flutter, no relapses of atrial arrhythmia were recorded during follow-up.

In this study, determining the clinical indicators that predict recurrent AF after two-staged correction of AF was impossible. This may be related to the following:

1) Absence of difference in the technique of the surgical correction of AF. Both groups underwent surgery using the LA cut-and-sew technique, and the BA group also underwent right atrial correction. The technique of the LA procedure was not different between the groups.

2) Small sample size. We hope that future studies will provide additional information on this issue.

However, the AF duration before stage 1 of AF correction (p = 0.074) and the method of the surgical correction of AF (p = 0.054) had comparable significance values (p = 0.074). Thus, increasing the sample size in subsequent studies may have positively affected changes in the indicators of the significance criterion.

DISCUSSION

Currently, the maze III procedure is considered a highly effective method of treating AF during combined cardiac interventions [6, 12, 13]. Despite the high efficiency of the BA procedure, no clear opinion is presented in the literature about the need for the fragmentation of the right atrium. Evidence shows that the simplified LA scheme of the maze III procedure is associated with postoperative tachyarrhythmias such as atrial fluttering in 8%–10% of cases [3]. In this study, a highly effective endocardial termination of macro re-entry tachycardias such as atrial fluttering was performed when the ablation line was closed in all cases. No recurrences of arrhythmias were recorded after the ablation of atrial flutter intraoperatively during arrhythmia induction and after 34.37 (standard deviation 24.32) months of follow-up.

Despite the use of the highly effective maze III technique, which virtually eliminates the risk of recurrent arrhythmias, in this study, both groups showed signs of recurrent AF and reconnection of conduction in the PVs. Among the published studies, some studies have confirmed the restoration of conduction in the veins after performing various modifications of maze III procedure [18–20]. In our opinion, the finding of the reconnection in the veins can be due to the following:

1. The actual use of the maze III technique with additional lines toward the fibrous ring of the tricuspid valve and mitral valve using the AtriCure cryoICE cryoablator (AtriCure, USA), which may cause the local recanalization of the conduction.

2. Many years of surgical skills gained in the surgical treatment of AF. When analyzing the timing of surgeries, patients who underwent the two-atrial "classical" maze technique with recurrences of conduction in the PVs had undergone surgery at the beginning of the FCHMT activities, which was at the stage of mastering the technique. Moreover, the LA maze modification was attributed to the implementation of experience and continuation of work for many years. We assumed that the transmurality of all effects (cut-and-sew and cryoablation lines) turned out to be more achievable with surgeons' acquisition of practical skills. Moreover, the endocardial re-isolation was segmental and easily achievable in all cases.

The study showed no differences in subsequent tachyarrhythmias depending on the method used for the surgical correction of AF during combined cardiac interventions. We believe that the high effectiveness of endocardial ablation of recurrent atrial arrhythmias demonstrated in this study (82.6% and 92.9% in groups 1 and 2, respectively) was associated with the presence of tachyarrhythmias with a regular tachycardia cycle, atrial fluttering, and atrial tachycardia in patients referred for ablation (32 of 39).

Thus, the lack of differences in the outcomes of surgical treatment between the groups may be due to the following factors:

1. Relatively small sample size. Our preliminary results should be confirmed by studies with larger sample sizes to describe better the negative effect of long persistent arrhythmia on rhythm maintenance after two-stage AF correction.

2. Important criteria for differences in groups were not considered, such as the degree of deformity and three-dimensional changes in atrial contractility based on the progressive speckle-tracking method of the ultrasound visualization of cardiac cavities. Although this new technique was introduced exclusively for the analysis of left ventricular function, several studies have recently expanded its application to other cardiac chambers, such as the left atrium [22]. Our subsequent work on assessing the maintenance of a regular atrial rhythm after two-stage AF correction will focus on the study of these parameters.

Based on the results of the analysis of factors that influence atrial rhythm after maze surgeries, the severity of structural and electrophysiological pathologies of the atria is the main cause of the recurrence of tachyarrhythmias despite the two-staged correction of long-term AF. In our opinion, the presence of AF after the maze procedure indicates significant electrophysiological changes in the structure of the atria, and is the main criterion for the impossibility of maintaining a regular atrial rhythm.

CONCLUSION

The results of a study conducted at the FCHMT demonstrate the high effectiveness of the hybrid approach in the treatment of AF. Stage 1 involved the surgical correction of AF and other cardiac interventions. Stage 2 included endocardial ablation of recurrent tachyarrhythmias. Options for surgical correction of AF were BA maze or only LA correction, which did not demonstrate significant differences in the incidence and type of recurrence of atrial tachyarrhythmias. The occurrence of AF after both types of maze surgery reduces the probability of the restoration and maintenance of sinus rhythm with repeated catheter procedures. Tachyarrhythmias with a regular arrhythmia cycle, namely, atrial flutter and atrial tachycardia, are prognostically favorable atrial arrhythmias for the restoration and long-term maintenance of a regular atrial rhythm.

ADDITIONAL INFORMATION

Authors' contribution. Thereby, all authors made a substantial contribution to the conception of the study, acquisition, analysis, interpretation of data for the work, drafting and revising the article, final approval of the version to be published and agree to be accountable for all aspects of the study. The contribution of each author: A.S. Postol — research concept and design, data collection and processing, text writing and editing, integration of all article parts; G.N. Antipov, V.V. Lyashenko — data collection, discussion of data obtained, text editing, statistical data analysis; A.V. Ivanchenko — data collection, concept of research parameters, data analysis; D.A. Kalinin — data collection, text and tables editing; S.N. Kotov, A.B. Vygovsky — statistical data analysis; Yu.A. Shneider — editing, approval of the final version of the article.

Funding source. This study was not supported by any external sources of funding.

Competing interests. The authors declare that they have no competing interests.

Consent for publication. Written consent was obtained from the patient's parents for publication of relevant medical information and all of accompanying images within the manuscript.

ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Участие авторов. Все авторы внесли существенный вклад в разработку концепции, проведение исследования и подготовку статьи, прочли и одобрили финальную версию перед публикацией. Вклад каждого автора: А.С. Постол — концепция и дизайн исследования, сбор и обработка материала, написание и редактирование текста, ответственность за целостность всех частей статьи; Г.Н. Антипов В.В. Ляшенко — сбор материала, обсуждение полученных данных, редактирование текста, статистическая обработка данных; А.В. Иванченко — сбор материала, концепция параметров исследования, обработка информации; В.В. Калинин — сбор материала, редактирование текста и таблиц; С.Н. Котов, А.Б. Выговский — статистическая обработка данных; Ю.А. Шнейдер — редактирование, утверждение окончательного варианта статьи.

Источник финансирования. Авторы заявляют об отсутствии внешнего финансирования при проведении исследования.

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Информированное согласие на публикацию. Авторы получили письменное согласие пациентов на публикацию медицинских данных.

REFERENCES

1. Arakelyan MG, Bockeria LA, Vasilieva EYu, et al. 2020 Clinical guidelines for atrial fibrillation and atrial flutter. *Russian Journal of Cardiology*. 2021;26(7):190–260. (In Russ.) DOI: 10.15829/1560-4071-2021-4594

2. Phan K, Xie A, Tsai Y-C, et al. Biatrial ablation vs. left atrial concomitant surgical ablation for treatment of atrial fibrillation: a meta-analysis. *Europace*. 2015;17(1):38–47. DOI: 10.1093/europace/euu220

3. Zheng S, Zhang H, Li Y, et al. Comparison of left atrial and biatrial maze procedure in the treatment of atrial fibrillation: A meta-analysis of clinical studies. *Thorac Cardiovasc Surg*. 2016;64(8):661–671. DOI: 10.1055/s-0035-1554941

4. Andersen KS, Grong K, Hoff P-I, Wahba A. Long-term follow-up after surgery for atrial fibrillation with concomitant open heart surgery. *Tidsskr Nor Laegeforen*. 2021;141(1). DOI: 10.4045/tidsskr.20.0279

5. Yurkulieva GA, Abdulkerimov ShM, Ispiryan AYu, et al. Comparative assessment of quality of life of patients with atrial fibrillation after surgical and interventional treatment methods. *Annaly aritmologii*. 2020;17(2):84–96. (In Russ.) DOI: 10.15275/annaritmol.2020.2.2

6. Revishvili AS, Serguladze SYu, Ezhova IV, et al. Rezul'taty khirurgicheskogo lecheniya izolirovannykh form fibrillyatsii predserdii s ispol'zovaniem modifitsirovannoi operatsii «labirint». *Annaly aritmologii*. 2012;9(3):31–39. (In Russ.)

7. Elesin DA, Bogachev-Prokof'ev AV, Romanov AB, et al. Thoracoscopic method in treatment of patients with atrial fibrillation. *Russian Journal of Cardiology and Cardiovascular Surgery*. 2013;6(4):3740. (In Russ.)

8. Cox JL, Schuessler RB, D'Agostino HJ, et al. The surgical treatment of atrial fibrillation. III. Development of a difinitive surgical procedure. *J Thorac Cardiovasc Surg*. 1991;101(4):569–583. DOI: 10.1016/S0022-5223(19)36684-X

9. Revishvili AS, Serguladze SYu, Kvasha BI, et al. Early and late outcomes of surgical treatment of lone atrial fibrillation using radiofrequency modification of maze procedure. *Journal of Arrhythmology*. 2016;(83):23–31. (In Russ.)

10. Bogachev-Prokofyev AV, Pivkin AN, Syrtseva YV, et al. Combinesd treatment of paroxysmal atrial fibrillation in patients with mitral valve disease: analysis of long-term outcomes. *Journal of Arrhythmology*. 2017;(87):16–22. (In Russ.)

11. Antipov GN, Postol AS, Kotov SN, et al. Comparison of biatrial and left atrial maze procedure in concomitant cardiac procedures. *Russian Journal of Cardiology and Cardiovascular Surgery*. 2020;13(1):17–23. (In Russ.) DOI: 10.17116/kardio20201301117

12. Cox JL, Churyla A, Malaisrie SC, et al. Hybrid maze procedure for long standing persistent atrial fibrillation. *Ann Thoracic Surg*. 2018;107(2):610–618. DOI: 10.1016/j.athoracsur.2018.06.064

13. Bisleri G, Rosati F, Bontempi L, et al. Hybrid approach for the treatment of long-standing persistent atrial fibrillation: Electrophysiological findings and clinical results. *Eur J Cardiothorac Surg*. 2013;44(5):919–923. DOI: 10.1093/ejcts/ezt115

14. Gaynor SL, Diato MD, Prasad SM, et al. A prospective, single-center clinical trial of modified Cox maze procedure with bipolar radiofrequency ablation. *J Thorac Cardiovasc Surg*. 2004;128(4):535–542. DOI: 10.1016/j.jtcvs.2004.02.044

15. Trumello C, Pozzoli A, Mazzone P, et al. Electrophysiological findings and long-term outcomes of percutaneous ablation of atrial arrhythmias after surgical ablation for atrial fibrillation. *Eur J Cardiothorac Surg*. 2016;49(1):273–280. DOI: 10.1093/ejcts/ezv034

16. Antipov GN, Postol AS, Kotov SN, et al. Analysis of the causes and frequency of permanent pacemaker implantation after different variants of surgical treatment of atrial fibrillation with combined cardiac surgery. *Clinical and Experimental Surgery. Petrovsky journal*. 2021;9(4):48–56. (In Russ.) DOI: 10.33029/2308-1198-2021-9-4-48-56

17. Lyashenko VV, Ivanchenko AV, Postol AS, et al. Electrophysiological mechanisms of arrhythmias after thoracoscopic Maze procedure. *Journal of Arrhythmology*. 2020;27(2):5–15. (In Russ.) DOI: 10.35336/VA-2020-2-5-15

18. Chun JKR, Bansch D, Ernst S, et al., Pulmonary vein conduction is the major finding in patients with atrial tachyarrhythmias after intraoperative maze ablation. *J Cardiovasc Electrophysiol*. 2007;18(4):358–363. DOI: 10.1111/j.1540-8167.2007.00771.x

19. Stasiuk YP. Comparison of monopolar and bipolar cox-maze ablation based on clinical data and mathematical modeling. *Vestnik NTU KPI. Seriya Radiotekhnika radioapparatostroeniya*. 2020;(83):55–61. (In Russ.)

20. Andersen KS, Grong K, Hoff P, Wahba A. Long-term follow-up after surgery for atrial fibrillation with concomitant open heart surgery. *Tidsskrift for Den norske legeforening*. 2021;141(1). DOI: 10.4045/tidsskr.20.0279

21. Mandoli GE, Pastore MC, Vasilijevaite K, et al. Speckle tracking stress echocardiography: A valuable diagnostic technique or a burden for everyday practice? *Echocardiography*. 2020;37(12):2123–2129. DOI: 10.1111/echo.14894

СПИСОК ЛИТЕРАТУРЫ

1. Аракелян М.Г., Бокерия Л.А., Васильева Е.Ю., и др. Фибрилляция и трепетание предсердий. Клинические рекомендации 2020 // Российский кардиологический журнал. 2021. Т. 26, № 7. С. 190–260. DOI: 10.15829/1560-4071-2021-4594

2. Phan K., Xie A., Tsai Y.-C., et al. Biatrial ablation vs. left atrial concomitant surgical ablation for treatment of atrial fibrillation: a meta-analysis // Europace. 2015. Vol. 17, No. 1. P. 38–47. DOI: 10.1093/europace/euu220

3. Zheng S., Zhang H., Li Y., et al. Comparison of left atrial and biatrial maze procedure in the treatment of atrial fibrillation: A meta-analysis of clinical studies // Thorac Cardiovasc Surg. 2016. Vol. 64, No. 8. P. 661–671. DOI: 10.1055/s-0035-1554941

4. Andersen K.S., Grong K., Hoff P.-I., Wahba A. Long-term follow-up after surgery for atrial fibrillation with concomitant open heart surgery // Tidsskr Nor Laegeforen. 2021. Vol. 141, No. 1. DOI: 10.4045/tidsskr.20.0279

5. Юркулиева Г.А., Абдулкеримов Ш.М., Испирян А.Ю., и др. Сравнительная оценка качества жизни пациентов с фибрилляцией предсердий после хирургического и интервенционного методов лечения // Анналы аритмологии. 2020. Т. 17, № 2. С. 84–96. DOI: 10.15275/annaritmol.2020.2.2

6. Ревишвили А.Ш., Сергуладзе С.Ю., Ежова И.В., и др. Результаты хирургического лечения изолированных форм фибрилляции предсердий с использованием модифицированной операции «лабиринт» // Анналы аритмологии. 2012. Т. 9, № 3. С. 31–39.

7. Елесин Д.А., Богачев-Прокофьев А.В., Романов А.Б., и др. Торакоскопический метод в лечении пациентов с фибрилляцией предсердий // Кардиология и сердечно-сосудистая хирургия. 2013. Т. 6, № 4. С. 3740.

8. Cox J.L., Schuessler R.B., D'Agostino H.J., et al. The surgical treatment of atrial fibrillation. III. Development of a difinitive surgical procedure // J Thorac Cardiovasc Surg. 1991. Vol. 101, No. 4. P. 569–583. DOI: 10.1016/S0022-5223(19)36684-X

9. Ревишвили А.Ш., Сергуладзе С.Ю., Кваша Б.И., и др. Ближайшие и отдаленные результаты хирургического лечения «изолированных» форм фибрилляции предсердий с помощью радиочастотной модификации операции «лабиринт-V» // Вестник аритмологии. 2016. № 83. С. 23–31.

10. Богачев-Прокофьев А.В., Пивкин А.Н., Сырцева Я.В., и др. Сочетанное лечение пароксизмальной фибрилляции предсердий у пациентов с пороками митрального клапана: анализ отдаленных результатов // Вестник аритмологии. 2017. № 87. С. 16–22.

11. Антипов Г.Н., Постол А.С., Котов С.Н., и др. Сравнение биатриальной и левопредсердной процедур «лабиринт» при сочетанных операциях на сердце // Кардиология и сердечно-сосудистая хирургия. 2020. Т. 13, № 1. С. 17–23. DOI: 10.17116/kardio20201301117

12. Cox J.L., Churyla A., Malaisrie S.C., et al. Hybrid maze procedure for long standing persistent atrial fibrillation // Ann Thoracic Surg. 2018. Vol. 107, No. 2. P. 610–618. DOI: 10.1016/j.athoracsur.2018.06.064

13. Bisleri G., Rosati F., Bontempi L., et al. Hybrid approach for the treatment of long-standing persistent atrial fibrillation: Electrophysiological findings and clinical results // Eur J Cardiothorac Surg. 2013. Vol. 44, No. 5. P. 919–923. DOI: 10.1093/ejcts/ezt115

14. Gaynor S.L., Diato M.D., Prasad S.M., et al. A prospective, single-center clinical trial of modified Cox maze procedure with bipolar radiofrequency ablation // J Thorac Cardiovasc Surg. 2004. Vol. 128, No. 4. P. 535–542. DOI: 10.1016/j.jtcvs.2004.02.044

15. Trumello C., Pozzoli A., Mazzone P., et al. Electrophysiological findings and long-term outcomes of percutaneous ablation of atrial arrhythmias after surgical ablation for atrial fibrillation // Eur J Cardiothorac Surg. 2016. Vol. 49, No. 1. P. 273–280. DOI: 10.1093/ejcts/ezv034

16. Антипов Г.Н., Постол А.С., Котов С.Н., и др. Анализ причин и частоты имплантации кардиостимуляторов после различных вариантов хирургического лечения фибрилляции предсердий при сочетанных операциях на сердце. Клиническая и экспериментальная хирургия // Журнал имени академика Б.В. Петровского. 2021. Т. 9, № 4. С. 48–56. DOI: 10.33029/2308-1198-2021-9-4-48-56

17. Ляшенко В.В., Иванченко А.В., Постол А.С., и др. Электрофизиологические механизмы аритмий после торакоскопической процедуры Maze // Вестник аритмологии. 2020. Т. 27, № 2. С. 5–15. DOI: 10.35336/VA-2020-2-5-15

18. Chun J.K.R., Bansch D., Ernst S., et al., Pulmonary vein conduction is the major finding in patients with atrial tachyarrhythmias after intraoperative maze ablation // J Cardiovasc Electrophysiol. 2007. Vol. 18, No. 4. P. 358–363. DOI: 10.1111/j.1540-8167.2007.00771.x

19. Стасюк Ю.П. Сравнение монополярной и биполярной абляции cox-maze на основе клинических данных и математического моделирования // Вестник НТУ КПИ. Серия Радиотехника радиоаппаратостроения. 2020. № 83. С. 55–61.

20. Andersen K.S., Grong K., Hoff P., Wahba A. Long-term follow-up after surgery for atrial fibrillation with concomitant open heart surgery // Tidsskrift for Den norske legeforening. 2021. Vol. 141, No. 1. DOI: 10.4045/tidsskr.20.0279

21. Mandoli G.E., Pastore M.C., Vasilijevaite K., et al. Speckle tracking stress echocardiography: A valuable diagnostic technique or a burden for everyday practice? // Echocardiography. 2020. Vol. 37, No. 12. P. 2123–2129. DOI: 10.1111/echo.14894

AUTHORS INFO

***Anzhelika S. Postol,** Cand. Sci. (Med.), doctor of arrhythmology department of the Federal Center for High Medical Technologies of Healthcare Ministry of Russia, Kaliningrad; Senior Lecturer of Therapy of Immanuel Kant Baltic Federal University, Kaliningrad, Russia; ORCID: 0000-0003-0983-3773; eLibrary SPIN: 1322-5069; e-mail: postol-75@mail.ru

Georgy N. Antipov, Cand. Sci. (Med.), Head of the Cardiosurgical Department No. 2 of the Federal Center for High Medical Technologies, Kaliningrad, Russia; ORCID: 0000-0002-7704-2669; eLibrary SPIN: 5399-9578; e-mail: enzo17@mail.ru

Andrei V. Ivanchenko, Head of the Department of Surgical Treatment of Complex Cardiac Arrhythmias and Electrocardiostimulation of the Federal Center for High Medical Technologies, Kaliningrad, Russia; ORCID: 0000-0001-5501-4926; e-mail: ivancha74@gmail.com

Vitaly V. Lyashenko, surgeon of Cardiovascular Surgeon Arrhythmology Department of the Federal Center for High Medical Technologies, Kaliningrad, Russia; ORCID: 0000-0002-8501-4801; eLibrary SPIN: 3023-3477; e-mail: vitalylyashenko5@gmail.com

Dmitriy A. Kalinin, surgeon of Cardiovascular Surgeon Arrhythmology Department of the Federal Center for High Medical Technologies, Kaliningrad, Russia; ORCID: 0000-0003-0942-3264; e-mail: dk.oniks@mail.ru

Sergey N. Kotov, Head of Functional Diagnostics Department of the Federal Center for High Medical Technologies, Kaliningrad, Russia; ORCID: 0000-0002-4027-4159; eLibrary SPIN: 2554-3369; e-mail: ksn82@rambler.ru

Alexander B. Vigovsky, Deputy Chief Physician for Medical Affairs of the Federal Center for High Medical Technologies, Kaliningrad, Russia; ORCID: 0000-0003-4832-2028; eLibrary SPIN: 2094-9955; e-mail: vygovsky@list.ru

Yuriy A. Schneider, MD, Dr. Sci. (Med.), Professor, Head of the Federal Center for High Medical Technologies, Kaliningrad, Russia; ORCID: 0000-0002-5572-3076; eLibrary SPIN: 5027-6453; e-mail: schneider@mail.ru

ОБ АВТОРАХ

***Анжелика Сергеевна Постол,** канд. мед. наук, врач отделения хирургического лечения сложных нарушений ритма сердца и электрокардиостимуляции Федерального центра высоких медицинских технологий, старший преподаватель кафедры терапии Балтийского федерального университета им. И. Канта, Калининград, Россия; ORCID: 0000-0003-0983-3773; elibrary SPIN: 1322-5069; e-mail: postol-75@mail.ru

Георгий Николаевич Антипов, канд. мед. наук, заведующий кардиохирургическим отделением № 2 Федерального центра высоких медицинских технологий, Калининград, Россия; ORCID: 0000-0002-7704-2669; eLibrary SPIN: 5399-9578; e-mail: enzo17@mail.ru

Андрей Владимирович Иванченко, заведующий отделением хирургического лечения сложных нарушений ритма сердца и электрокардиостимуляции Федерального центра высоких медицинских технологий, Калининград, Россия; ORCID: 0000-0001-5501-4926; e-mail: ivancha74@gmail.com

Виталий Валерьевич Ляшенко, врач сердечно-сосудистый хирург отделения, Федерального центра высоких медицинских технологий, Калининград, Россия; ORCID: 0000-0002-8501-4801; eLibrary SPIN: 3023-3477; e-mail: vitalylyashenko5@gmail.com

Дмитрий Александрович Калинин, врач сердечно-сосудистый хирург отделения хирургического лечения сложных нарушений ритма сердца и электрокардиостимуляции Федерального центра высоких медицинских технологий, Калининград, Россия; ORCID: 0000-0003-0942-3264; e-mail: dk.oniks@mail.ru

Сергей Николаевич Котов, заведующий отделением функциональной диагностики Федерального центра высоких медицинских технологий, Калининград, Россия; ORCID: 0000-0002-4027-4159; eLibrary SPIN: 2554-3369; e-mail: ksn82@rambler.ru

Александр Борисович Выговский, заместитель главного врача по медицинской части Федерального центра высоких медицинских технологий, Калининград, Россия; ORCID: 0000-0003-4832-2028; eLibrary SPIN: 2094-9955; e-mail: vygovsky@list.ru

Юрий Александрович Шнейдер, д-р мед. наук, заслуженный врач России, профессор, главный врач Федерального центра высоких медицинских технологий, Калининград, Россия; ORCID: 0000-0002-5572-3076; eLibrary SPIN: 5027-6453; e-mail: schneider@mail.ru

* Corresponding author / Автор, ответственный за переписку

DOI: https://doi.org/10.17816/cardar567797

Reseach article

Atrial fibrillation in a patient with diffuse myocardial fibrosis and mitral annular disjunction

Larisa S. Evdokimova, Irina E. Itskovich, Tatiana N. Novikova, Tatyana V. Garpinchenko

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

Abstract

A case of atrial fibrillation and premature ventricular complexes (PVC) in a patient with mitral valve prolapse and mitral annular disjunction is described. Rhythm disturbances occurred after a new coronavirus infection. Also, the patient has a history of combined treatment of left breast cancer, which contributed to the appearance of myocardial fibrosis as an arrhythmogenic substrate. Due to the ineffectiveness of conservative antiarrhythmic therapy, a radiofrequency catheter procedure was performed, which proved unsuccessful. The purpose of the article is to present the possible causes of cardiac arrhythmias and the role of magnetic resonance imaging in the diagnosis of arrhythmogenic myocardial fibrosis and mitral annular disjunction.

Keywords: atrial fibrillation; mitral annular disjunction; postradiation myocardial fibrosis; cardiac MRI.

To cite this article

Evdokimova LS, Itskovich IE, Novikova TN, Garpinchenko TV. Atrial fibrillation in a patient with diffuse myocardial fibrosis and mitral annular disjunction. *Cardiac Arrhythmias.* 2023;3(3):19–26. DOI: https://doi.org/10.17816/cardar567797

Received: 27.07.2023 **Accepted:** 24.09.2023 **Published:** 10.11.2023

DOI: https://doi.org/10.17816/cardar567797

Научная статья

Фибрилляция предсердий у пациентки с диффузным фиброзом миокарда и митральной аннулярной дизъюнкцией

Л.С. Евдокимова, И.Э. Ицкович, Т.Н. Новикова, Т.В. Гарпинченко

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

Аннотация

Описано наблюдение случая фибрилляции предсердий и желудочковой экстрасистолии у пациентки с пролапсом митрального клапана и митральной аннулярной дизъюнкцией. Дебют нарушений ритма инициирован перенесенной новой коронавирусной инфекцией. Кроме того, в анамнезе пациентки комбинированное лечение рака левой молочной железы, способствовавшее появлению фиброза миокарда в качестве аритмогенного субстрата. В связи с неэффективностью консервативной антиаритмической терапии была выполнена радиочастотная катетерная процедура по поводу симптомной фибрилляции предсердий, оказавшаяся безуспешной. Цель статьи — представить возможные причины возникновения нарушений ритма сердца и роль магнитно-резонансной томографии в диагностике аритмогенного фиброза миокарда и митральной аннулярной дизъюнкции.

Ключевые слова: фибрилляция предсердий; митральная аннулярная дизъюнкция; постлучевой фиброз миокарда; МРТ сердца.

Как цитировать

Евдокимова Л.С., Ицкович И.Э., Новикова, Т.Н. Гарпинченко Т.В. Фибрилляция предсердий у пациентки с диффузным фиброзом миокарда и митральной аннулярной дизъюнкцией // Cardiac Arrhythmias. 2023. Т. 3, № 3. С. 19–26. DOI: https://doi.org/10.17816/cardar567797

Рукопись получена: 27.07.2023 **Рукопись одобрена:** 24.09.2023 **Опубликована:** 10.11.2023

ЭКО•ВЕКТОР

CLINICAL CASE

Patient D (59 years old) was admitted to the hospital for radiofrequency ablation (RFA) for atrial fibrillation (AF). The disease began in December 2020, when paroxysmal AF was first reported during inpatient treatment for pneumonia caused by moderate COVID-19. Another AF episode requiring hospitalization occurred in November 2022. Sinus rhythm was restored by electrical impulse therapy; however, after 4 days, arrhythmia recurred without subsequent restoration of sinus rhythm. AF was accompanied by symptoms such as dyspnea, asthenia, and palpitations; therefore, RFA (pulmonary vein isolation) was recommended.

Upon admission for RFA for AF, the patient had palpitations and interruptions in cardiac function, accompanied by dyspnea and asthenia, both during physical activity and at rest. The history of combined treatment for cancer of the left breast in 2004 (left-sided mastectomy, chemotherapy, and radiation therapy) was noteworthy. The concomitant disease was diffuse nodular goiter (euthyroidism on hormone replacement therapy). The patient was constantly taking bisoprolol (2.5 mg), L-thyroxine (75 mg), and rivaroxaban (20 mg).

Objective status on admission showed a satisfactory state, vesicular breathing, and absence of wheezing. Heart sounds were arrhythmic, the heart and pulse rates were 66 beats/min, and the blood pressure was 100/70 mmHg. The abdomen was soft and painless on palpation. No peripheral edema was observed.

Preoperatively, laboratory and instrumental diagnostic methods were performed. The values of clinical and biochemical blood test indicators were within the reference values.

During the inpatient treatment preceding this hospitalization, coronary angiography revealed the absence of stenotic or occlusive lesions of the coronary arteries.

The results of the electrocardiography (ECG) are presented in Fig. 1. The ECG recorded AF, ventricular extrasystole (VE), and QRS morphology characteristic of ventricular rhythm disorders from the outflow tract of the right ventricle (RV) that was atypical for mitral valve prolapse (MVP) and mitral annular disjunction (MAD). The presence of right VE may be associated with diffuse postradiation myocardial fibrosis, affecting not only the left ventricle (LV) but also the RV. Subsequently, repeated ECGs also recorded AF and VE of similar morphology.

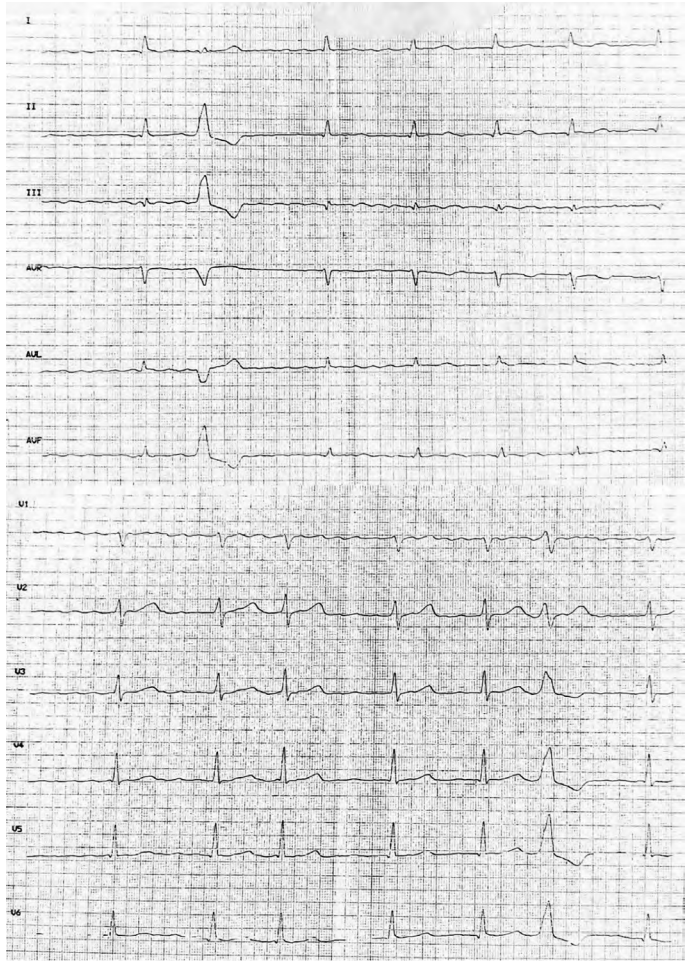


Fig. 1. Electrocardiogram (50 mm/s, 10 mm/mV). Atrial fibrillation, normosystolic form. Single ventricular extrasystole
Рис. 1. Электрокардиограмма (50 мм/с, 10 мм/мВ). Фибрилляция предсердий, нормосистолическая форма. Одиночная желудочковая экстрасистола

DOI: https://doi.org/10.17816/cardar567797

The patient first learned about the presence of MVP and MAD during the examination that preceded RFA. Echocardiography (echoCG) did not reveal local impairment of the contractility of the left ventricular myocardium, and the myocardium was not thickened. Moderate myxomatous changes in the mitral valve cusps and grade 1 mitral regurgitation with a volume of up to 10 mL were observed, and the disjunction of the mitral valve ring was located up to 8 mm. The main parameters of echoCG and magnetic resonance imaging (MRI) are presented in Table 1.

To clarify the size of the cardiac chambers, contractile function of the left ventricular myocardium, and presence of myocardial fibrosis, cardiac MRI was performed with the intravenous administration of the contrast agent (CA) gadodiamide (0.2 mmol/kg). The study was conducted according to a standard scanning protocol with native T1 mapping of the myocardium. In addition to echoCG data, attention was drawn to the beginning hypertrophy of the lower basal segments of the left ventricular myocardium, a decrease in ejection fraction (EF) to 46%, and mild hypokinesia of the apical segments (Table 1). The difference in EF according to the results of the two methods can be due to cardiac arrhythmia and by different postprocessing calculation methods. As with MRI, more than 300 MRI slices were included in cardiac cycles of different durations, which led to a greater spread of EF in different cycles than with echoCG, during which 3–5 cycles were taken to calculate the EF. The difference between the EF measured using different imaging techniques can sometimes reach 20% [1]. In the presented case, the authors took the echoCG data obtained as the true EF values because of high accessibility for dynamic monitoring.

Prolapse of both cusps of the MV and MAD up to 8 mm at the level of the P3 segment was visualized (Fig. 2).

When analyzing the qualitative and quantitative indicators of native T1 mapping (modified Look–Locker inversion recovery), areas where the T1 relaxation time of the myocardium of the interventricular septum and anterior and lateral walls of the LV was increased were identified, which were more pronounced at the level of the apical and middle segments (Fig. 3). In a quantitative analysis, the relaxation time in the indicated areas was > 1200 ms (above the average norm for 3.0 T tomographs of 1122 ± 57 ms) [4]. Taking into account previous radiation therapy for left breast cancer, these areas are manifestations of diffuse myocardial fibrosis.

After intravenous CA administration in the delayed phase (myocardial delayed enhancement), an extended area of intramural accumulation of a nonischemic CA was identified and localized in the lower and posterolateral segments (4, 5) of the left ventricular basal sections (Figs. 4 and 5). No focal accumulation of CA was noted in areas with increased T1 relaxation time.

During the electrophysiological study against AF, an anatomical and activation map of the LA was constructed, according to which pathological activity was identified in the area of the left inferior pulmonary vein. The ostia of the pulmonary veins were isolated, followed by electrical pulse therapy. Unfortunately, sinus rhythm could not be restored.

After the correction of drug therapy, the patient was discharged in satisfactory condition with recommendations for further follow-up by a rhythmologist and RFA for ventricular arrhythmias if drug therapy was ineffective.

DISCUSSION

The onset of cardiac arrhythmias in the patient was recorded during hospitalization for COVID-19; however, the infectious disease cannot be regarded as the only cause of AF. A study [5] provided data on factors predisposing to paroxysmal AF in individuals hospitalized for COVID-19, including older age, cardiovascular disease, increased left atrial volume, and severity of COVID-19. The patient was

Table 1. The main parameters obtained by echocardiography and cardiac MRI
Таблица 1. Основные параметры по результатам эхокардиографии и магнитно-резонансной томографии сердца

Parameters	EchoCG (B-mode) (range of normal values) [2]	MRI of the heart (range of normal values) [3]
LVEF, %	60 (54–74)	46 (59–77)
LV EDV, mL	99 (46–106)	106 (86–166)
LV ESV, mL	39 (14–42)	58 (22–59)
Indexed LV EDV, mL/m^2	56 (29–61)	59 (56–90)
Indexed LV ESV, mL/m^2	22 (8–24)	32 (14–33)
Myocardial mass, g	132 (67–162)	95 (72–144)
Indexed myocardial mass, g/m^2	75 (43–94)	52 (48–78)
Indexed LA volume, mL/m^2	50 (16–34)	57 (27–53)

Note: EDV — end-diastolic volume; echoCG — echocardiography; ESV — end-systolic volume; LA — left atrium; LVEF — left ventricular ejection fraction; MRI — magnetic resonance imaging.
Примечание: ФВ ЛЖ — фракция выброса левого желудочка; КДО — конечно-диастолический объем; КСО — конечно-систолический объем; ЛП — левое предсердие.

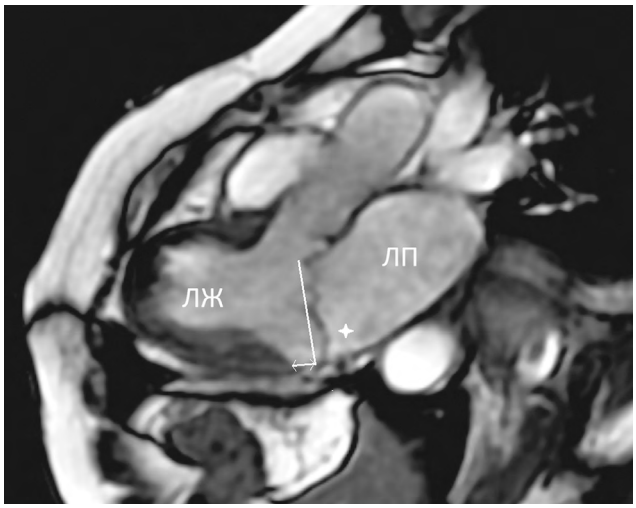


Fig. 2. Cardiac MRI, of end-systolic image in three-chamber view (Fiesta Cine). The thick arrow indicates the prolapse of the posterior leaf of the MV, the projection axis of the fibrous ring of the MV is carried out, the bidirectional arrow indicates the distance of the mitral annular disjunction

Рис. 2. Магнитно-резонансная томография сердца, конечно-систолическое изображение в трехкамерном виде (Fiesta Cine). Толстая стрелка указывает на пролапс задней створки митрального клапана, проведена проекционная ось фиброзного кольца митрального клапана, двунаправленная стрелка указывает расстояние митральной аннулярной дизъюнкции

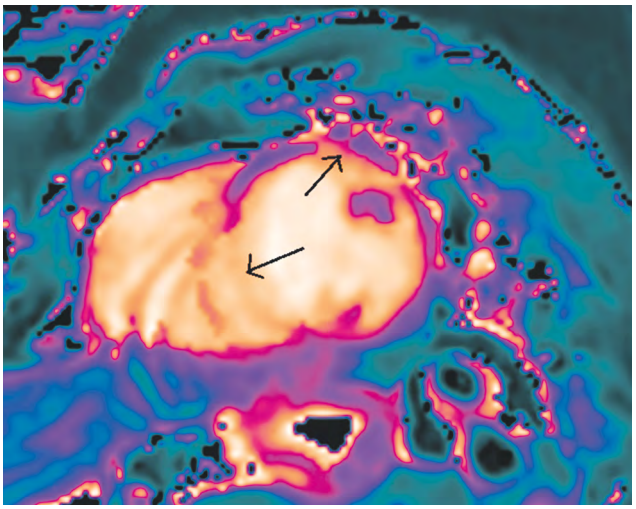


Fig. 3. Cardiac MRI, T1-mapping short axis of the left ventricle. The arrows indicate areas with increased T1-relaxation time localized in the interventricular septum and in the anterior wall of the left ventricle at the level of the apical segments

Рис. 3. Магнитно-резонансная томография сердца, Т1-картирование миокарда по короткой оси левого желудочка. Стрелки указывают области с повышенным временем Т1-релаксации, локализованные в межжелудочковой перегородке и в передней стенке левого желудочка на уровне начала срединных сегментов

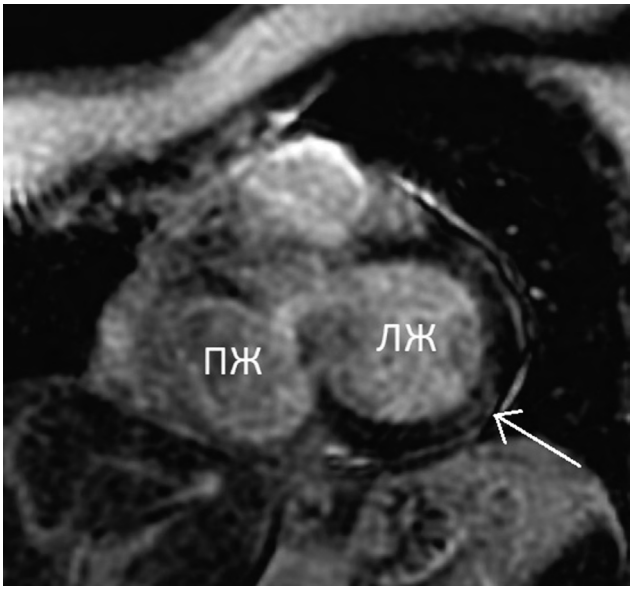


Fig. 4. Cardiac MRI, short axis at the level of the basal segments. Late gadolinium enhancement. The arrow indicates an intramural non-ischemic zone of contrast accumulation at the border of 4 and 5 left ventricle segments. ПЖ — right ventricle; ЛЖ — left ventricle

Рис. 4. Магнитно-резонансная томография сердца, по короткой оси на уровне базальных сегментов. Отсроченное контрастирование. Стрелкой указан интрамуральный участок накопления контрастного вещества на границе 4-го и 5-го сегментов левого желудочка неишемического характера. ПЖ — правый желудочек; ЛЖ — левый желудочек

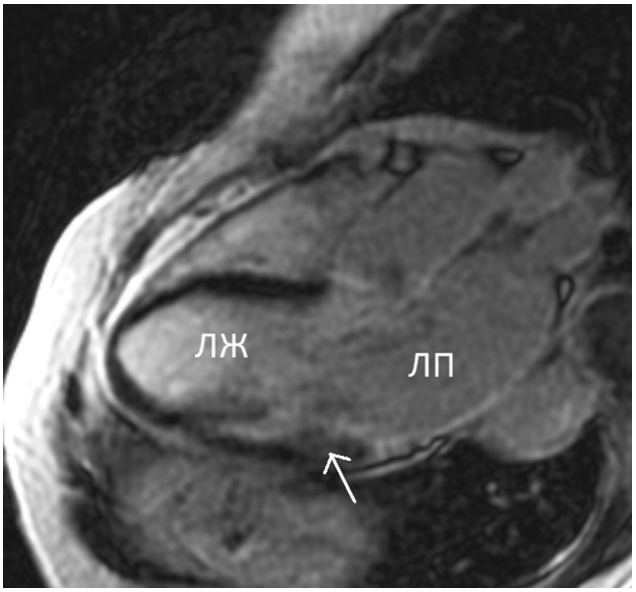


Fig. 5. Cardiac MRI. Three-chamber view. Late gadolinium enhancement. The arrow indicates a low-intensity intramural zone of contrast accumulation at the level of 5th segment left ventricle. ЛЖ — left ventricle; ЛП — left atrium

Рис. 5. Магнитно-резонансная томография сердца. Трехкамерный вид. Отсроченное контрастирование. Стрелкой указан слабоинтенсивный интрамуральный участок накопления контрастного вещества на уровне 5-го сегмента левого желудочка. ЛЖ — левый желудочек; ЛП — левое предсердие

DOI: https://doi.org/10.17816/cardar567797

59 years old, and the average age of patients in the study was 75.9 ± 2.3 years. The course of COVID-19 was moderately severe. Among the two listed moderate risk factors, an increase in the left atrial volume index contributed to the emergence of AF. Several reasons were identified for the left atrial remodeling in the patient. First, MVP and MAD were present. Diffuse postradiation myocardial fibrosis involving not only the ventricular myocardium but also the atrial myocardium not only played an important role in AF onset but was also, perhaps, the key factor in the ineffectiveness of RFA [6].

Presumably, according to the QRS morphology, the ectopic focus of the ventricular activity in our patient was located in the right ventricular outflow tract; however, it was not possible to identify the substrate of ventricular ectopy using MRI. The assessment of fibrotic changes in the RV still poses a certain challenge because of the small thickness of the right ventricular wall, diffuse interstitial changes that are difficult to visualize even using T1 mapping of the myocardium, and delayed contrast sensitivity to fibrotic changes involving >1 g of the myocardium [7].

The assessment of left ventricular myocardial fibrosis using MRI is a different matter. In the present case, another tool that was used to assess the presence of diffuse myocardial fibrosis of the LV was the measurement of the T1 relaxation time using MRI. The method was based on mapping to assess qualitatively (using color coding of the relaxation time) and quantitatively (measuring directly the relaxation time) changes in the myocardium. Postcontrast T1 mapping was used to calculate the extracellular volume reflecting diffuse myocardial fibrosis or accumulation of pathological substances in storage diseases. In the present study, the extracellular volume was not calculated because of rhythm disorder, and the presence of diffuse postradiation fibrosis was concluded based on native T1 mapping data and the absence of fields of focal accumulation of CA on delayed postcontrast images. Tuohinen et al. [8] noted that radiation therapy for left breast cancer led to an increase in the T1 relaxation time of the left ventricular myocardium with a predominantly apical and inferior septal gradient of changes, which reflects diffuse fibrosis, as in our case.

The results of delayed contrast enhancement and analysis of cine images proved the presence of MVP, MAD, and inferior basal intramural fibrosis of the LV in the patient. In the literature, this combination is called the “malignant triad” [9]. These changes, sometimes accompanied by hypertrophy of the lower basal segments of the left ventricular myocardium, predispose the patient to the development of ventricular arrhythmias (ventricular tachycardia and extrasystoles) and increase the risk of sudden cardiac death [10].

The relationship between MVP and MAD in the patient with AF may be due to left atrial remodeling caused by these conditions. In addition to local myocardial fibrosis, chronic MAD may be accompanied by diffuse myocardial fibrosis, which contributes to an additional load on the LA during diastole and left atrial remodeling [10].

In this patient, the myocardial fibrosis had several causes. At present, no universal diagnostic tools and methods would enable us to determine the association of fibrosis with a specific cause. In some areas of the patient’s myocardium, fibrosis was caused by radiation therapy, whereas in other areas, fibrosis was due to MVP and MAD that developed in parallel with postradiation fibrosis. The true causes of fibrosis in various areas of the myocardium remain to be speculated. The potential influence of the patient’s hormonal status is particularly noteworthy. Therefore, thyroid imbalance has minimal contribution to cardiac arrhythmias in euthyroidism.

CONCLUSION

The described clinical case demonstrates the capabilities of cardiac MRI in the diagnosis of left ventricular myocardial fibrosis of various causes. The detection of myocardial fibrosis and assessment of its distribution and volume are important for understanding the pathogenesis of rhythm disorders and assessing the potential effectiveness of therapy. In addition, cardiac MRI enables the determination of the parameters of contractile function and morphological changes in the LV. In some cases, its data are more accurate than transthoracic echoCG [11].

Unfortunately, currently, no technique can unambiguously assess left atrial myocardial fibrosis, which, in our opinion, causes the failure of not only drug therapy for AF but also RFA. The emergence of such techniques in the future will enable us to predict the efficiency and feasibility of catheterization procedures for AF.

ADDITIONAL INFORMATION

Competing interests. The authors declare that they have no competing interests.

Funding source. This study was not supported by any external sources of funding.

Consent and anonymity of the patient. The patient provided consent for anonymous use and publication of his medical data.

ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Источник финансирования. Авторы заявляют об отсутствии внешнего финансирования при проведении исследования.

Согласие и анонимность пациента. Пациент дал согласие на анонимное использование и публикацию своих медицинских данных.

REFERENCES

1. Pellikka PA, She L, Holly TA, et al. Variability in ejection fraction measured by echocardiography, gated single-photon emission computed tomography, and cardiac magnetic resonance in patients with coronary artery disease and left ventricular dysfunction. *JAMA Netw Open*. 2018;1(4):e181456. DOI: 10.1001/jamanetworkopen.2018.145

2. Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: An update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr*. 2015;28(1):1–39.E14. DOI: 10.1016/j.echo.2014.10.003

3. Herzog BA, Greenwood JP, Plein S, et al editors. *Cardiovascular magnetic resonance: Pocket guide. 2nd edition*. European Society of Cardiology, 2017. 119 p.

4. Roy C, Slimani A, de Meester C, et al. Age and sex corrected normal reference values of T1, T2, T2* and ECV in healthy subjects at 3T CMR. *J Cardiovasc Magn Reson*. 2017;19(1):72. DOI: 10.1186/s12968-017-0371-5

5. Podzolkov VI, Tarzimanova AI, Bragina AE, et al. Predictors of atrial fibrillation in patients with COVID-19. *Russian Journal of Cardiology*. 2022;27(7):29–35. (In Russ.) DOI: 10.15829/1560-4071-2022-5095

6. Suksaranjit P, Akoum N, Kholmovski EG, et al. Incidental LV LGE on CMR imaging in atrial fibrillation predicts recurrence after ablation therapy. *JACC: Cardiovasc Imaging*. 2015;8(7):793–800. DOI: 10.1016/j.jcmg.2015.03.008

7. Liang K, Nakou E, Del Buono MG, et al. The role of cardiac magnetic resonance in myocardial infarction and non-obstructive coronary arteries. *Front Cardiovasc Med*. 2022;8:821067. DOI: 10.3389/fcvm.2021.821067

8. Tuohinen S, Skytta T, Virtanen V, et al. Radiotherapy-induced changes in breast cancer patients in extra cellular volume and T1 mapping in cardiac magnetic resonance imaging and in ECG six years after radiotherapy treatment. *Eur Heart J – Cardiovasc Imaging*. 2019;20(S2):jez111.008. DOI: 10.1093/ehjci/jez111.008

9. Johnson JN, Mandell JG, Christopher A, et al. Society for Cardiovascular Magnetic Resonance 2020 case of the week series. *J Cardiovasc Magn Reson*. 2021;23:108. DOI: 10.1186/s12968-021-00799-0

10. Chakrabarti AK, Bogun F, Liang JJ. Arrhythmic mitral valve prolapse and mitral annular disjunction: Clinical features, pathophysiology, risk stratification, and management. *J Cardiovasc Dev Dis*. 2022;9(2):61. DOI: 10.3390/jcdd9020061

11. Novikova TN, Basova VA, Evdokimova LS, et al. A case of mitral annular disjunction combined with ventricular arrhythmias. *Cardiac Arrhythmias*. 2022;2(2):41–50. (In Russ.) DOI: 10.17816/cardar109160

СПИСОК ЛИТЕРАТУРЫ

1. Pellikka P.A., She L., Holly T.A., et al. Variability in ejection fraction measured by echocardiography, gated single-photon emission computed tomography, and cardiac magnetic resonance in patients with coronary artery disease and left ventricular dysfunction // JAMA Netw Open. 2018. Vol. 1, No. 4. ID e181456. DOI: 10.1001/jamanetworkopen.2018.145

2. Lang R.M., Badano L.P., Mor-Avi V., et al. Recommendations for cardiac chamber quantification by echocardiography in adults: An update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging // J Am Soc Echocardiogr. 2015. Vol. 28, No. 1. P. 1–39.E14. DOI: 10.1016/j.echo.2014.10.003

3. Cardiovascular magnetic resonance: Pocket guide. 2nd edition / B.A. Herzog, J.P. Greenwood, S. Plein, et al editors. European Society of Cardiology, 2017. 119 p.

4. Roy C., Slimani A., de Meester C., et al. Age and sex corrected normal reference values of T1, T2, T2* and ECV in healthy subjects at 3T CMR // J Cardiovasc Magn Reson. 2017. Vol. 19, No. 1. ID 72. DOI: 10.1186/s12968-017-0371-5

5. Подзолков В.И., Тарзиманова А.И., Брагина А.Е., и др. Предикторы возникновения фибрилляции предсердий у больных с коронавирусной инфекцией SARS-CoV-2 (COVID-19). // Российский кардиологический журнал. 2022. Т. 27, № 7. С. 29–35. DOI: 10.15829/1560-4071-2022-5095

6. Suksaranjit P., Akoum N., Kholmovski E.G., et al. Incidental LV LGE on CMR imaging in atrial fibrillation predicts recurrence after ablation therapy // JACC: Cardiovasc Imaging. 2015. Vol. 8, No. 7. P. 793–800. DOI: 10.1016/j.jcmg.2015.03.008

7. Liang K., Nakou E., Del Buono M.G., et al. The role of cardiac magnetic resonance in myocardial infarction and non-obstructive coronary arteries // Front Cardiovasc Med. 2022. Vol. 8. ID 821067. DOI: 10.3389/fcvm.2021.821067

8. Tuohinen S., Skytta T., Virtanen V., et al. Radiotherapy-induced changes in breast cancer patients in extra cellular volume and T1 mapping in cardiac magnetic resonance imaging and in ECG six years after radiotherapy treatment // Eur Heart J – Cardiovasc Imaging. 2019. Vol. 20, No. S2. ID jez111.008. DOI: 10.1093/ehjci/jez111.008

9. Johnson J.N., Mandell J.G., Christopher A., et al. Society for Cardiovascular Magnetic Resonance 2020 case of the week series // J Cardiovasc Magn Reson. 2021. Vol. 23. ID 108. DOI: 10.1186/s12968-021-00799-0

10. Chakrabarti A.K., Bogun F., Liang J.J. Arrhythmic mitral valve prolapse and mitral annular disjunction: Clinical features, pathophysiology, risk stratification, and management // J Cardiovasc Dev Dis. 2022. Vol. 9, No. 2. ID 61. DOI: 10.3390/jcdd9020061

11. Новикова Т.Н., Басова В.А., Евдокимова Л.С., и др. Случай митральной аннулярной дизъюнкции в сочетании с желудочковыми нарушениями ритма // Cardiac Arrhythmias. 2022. Т. 2, № 2. С. 41–50. DOI: 10.17816/cardar109160

AUTHORS INFO

***Larisa S. Evdokimova,** radiologist of the MRI room of the clinic, E.E. Eichwald North-Western State Medical University named after I.I. Mechnikov, Saint Petersburg, Russia;
ORCID: 0000-0002-7731-0109; eLibrary SPIN: 3780-9470;
e-mail: Larisa.Evdokimova@szgmu.ru

Irina E. Itskovich, Dr. Sci. (Med.), professor;
ORCID: 0000-0001-8352-3955; eLibrary SPIN: 1240-9338;
e-mail: itskovichirina@mail.ru

Tatiana N. Novikova, Cand. Sci. (Med.), associate professor;
ORCID: 0000-0003-4655-0297; eLibrary SPIN: 3401-0329;
e-mail: novikova-tn@mail.ru

TatyanaV. Garpinchenko, cardiologist;
ORCID: 0000-0002-5293-5647; eLibrary SPIN: 2396-2582;
e-mail: tatyana.garpinchenko@szgmu.ru

ОБ АВТОРАХ

***Лариса Сергеевна Евдокимова,** врач-рентгенолог кабинета МРТ клиники им. Э.Э. Эйхвальда Северо-Западного государственного медицинского университета
им. И.И. Мечникова, Санкт-Петербург, Россия;
ORCID: 0000-0002-7731-0109; eLibrary SPIN: 3780-9470;
e-mail: Larisa.Evdokimova@szgmu.ru

Ирина Эммануиловна Ицкович, д-р мед. наук, профессор;
ORCID: 0000-0001-8352-3955; eLibrary SPIN: 1240-9338;
e-mail: itskovichirina@mail.ru

Татьяна Николаевна Новикова, канд. мед. наук, доцент;
ORCID: 0000-0003-4655-0297; eLibrary SPIN: 3401-0329;
e-mail: novikova-tn@mail.ru

Татьяна Владимировна Гарпинченко, врач-кардиолог;
ORCID: 0000-0002-5293-5647; eLibrary SPIN: 2396-2582;
e-mail: tatyana.garpinchenko@szgmu.ru

* Corresponding author / Автор, ответственный за переписку

DOI: https://doi.org/10.17816/cardar568180

Reseach article

Clinical and genetic characterization of patients with catecholaminergic polymorphic ventricular tachycardia: a case series

Svetlana M. Komissarova[1], Nadiia M. Rineiska[1], Natalya N. Chakova[2], Svetlana N. Niyazova[2], Larisa I. Plashchinskaya[1], Veronika Ch. Barsukevich[1], Olga V. Podpalova[1]

[1] State Institution Republican Scientific and Practical Centre "Cardiology", Minsk, Belarus;

[2] Institute of Genetics and Cytology of Belarus National Academy of Sciences, Minsk, Belarus

Abstract

AIM: of the study was to evaluate the clinical and genetic characteristics, including the development of adverse events and outcomes in patients with catecholaminergic polymorphic ventricular tachycardia (CPVT).

MATERIALS AND METHODS: The clinical phenotype of eight patients with CPVT, two of whom were relatives of probands, was observed over 4 years. The clinical and instrumental study included ECG-12, 24-hour Holter ECG monitoring, genealogical history collection and family history of sudden cardiac death (SCD), transthoracic echocardiography and cardiac magnetic resonance imaging to detect structural myocardial changes, electrophysiologic study according to indications, and ICD monitoring. High-throughput sequencing (NGS) was utilized to search for mutations in genes linked to the onset of channelopathies and other inherited rhythm disorders.

RESULTS: In 8 patients, nucleotide variants of pathogenicity classes III-V were identified according to the ACMG (2015) criteria in the *RYR2* gene associated with CPVT. Pathogenic (IV-V class) and likely pathogenic (IV class) mutations in the *RYR2* gene were found in 6 (75%) probands, variants with uncertain clinical significance (VUS, class III) were found in 2 patients. At the time of diagnosis, transient QTc interval prolongation of more than 480 ms was detected in 4 (50%) patients; bradycardia less than 54 beats/min — in 2 (25%) patients, sequences of supraventricular tachycardia and ventricular tachyarrhythmia — in 2 (25%) patients. The most severe form of the disease with marked clinical manifestations and an episode of clinical death with subsequent resuscitation, as well as a transient QTc interval prolongation exceeding 500 ms was observed in patients with mutations c.11814C > A (p.Ser3938Arg, rs794728704); c.463G > A (p.Gly155Arg) and c.14876G > A (p.Arg4959Gln, rs794728811) in the *RYR2* gene. Three (37.5%) patients underwent ICD implantation; one for primary SCD prevention and two for secondary prevention.

CONCLUSION: In this study, the spectrum of clinical manifestations in patients with genetically confirmed CPVT was examined. The findings highlight transient QTc interval extensions, significant sinus bradycardia, and sequences of supraventricular tachyarrhythmias, which can escalate into life-threatening ventricular tachyarrhythmias in CPVT patients.

Keywords: catecholaminergic polymorphic ventricular tachycardia; *RYR2* gene mutation; phenotypic diversity.

To cite this article

Komissarova SM, Rineiska NM, Chakova NN, Niyazova SN, Plashchinskaya LI, Barsukevich VCh, Podpalova OV. Clinical and genetic characterization of patients with catecholaminergic polymorphic ventricular tachycardia: a case series. *Cardiac Arrhythmias.* 2023;3(3):27–40. DOI: https://doi.org/10.17816/cardar568180

Received: 09.08.2023 **Accepted:** 10.10.2023 **Published:** 10.11.2023

DOI: https://doi.org/10.17816/cardar568180

Научная статья

Клиническая и генетическая характеристика пациентов с катехоламинергической полиморфной желудочковой тахикардией (серия случаев)

С.М. Комиссарова[1], Н.М. Ринейская[1], Н.Н. Чакова[2], С.С. Ниязова[2], Л.И. Плащинская[1], В.Ч. Барсукевич[1], О.В. Подпалова[1]

[1] Республиканский научно-практический центр «Кардиология», Минск, Республика Беларусь;

[2] Институт генетики и цитологии НАН Беларуси, Минск, Республика Беларусь

Аннотация

Цель исследования — оценить клиническую и генетическую характеристику, включая развитие неблагоприятных событий и исходов у пациентов с катехоламинергической полиморфной желудочковой тахикардией (КПЖТ).

Материалы и методы. Обследовано 8 пациентов с КПЖТ, двое из которых были родственниками пробандов, наблюдаемых в течение 4 лет. Клинико-инструментальное исследование включало регистрацию электрокардиограммы в 12 отведениях, суточное электрокардиографическое мониторирование, сбор генеалогического анамнеза и выявление случаев внезапной сердечной смерти в семье или наличия семейной формы заболевания, эхокардиографическое исследование и магнитно-резонансную томографию сердца для исключения структурных изменений миокарда, проведение эндокардиального электрофизиологического исследования по показаниям, мониторинг имплантируемого кардиовертера-дефибриллятора. Поиск мутаций в кодирующих последовательностях генов, ассоциированных с развитием каналопатий и других наследственных нарушений ритма, проводили методом высокопроизводительного секвенирования.

Результаты. У 8 пациентов выявлены нуклеотидные варианты III–V классов патогенности согласно критериям ACMG (2015) в гене *RYR2*, ассоциированным с КПЖТ. У 6 (75 %) пробандов обнаружены диагностически значимые мутации (IV–V класса патогенности) в гене *RYR2*, у 2 пациентов были обнаружены варианты с неопределенной клинической значимостью (VUS, III класс). На момент постановки диагноза транзиторное удлинение интервала *QTc* более 480 мс было выявлено у 4 (50 %) пациентов; брадикардия менее 54 уд/мин — у 2 (25 %), суправентрикулярная тахикардия, которая сменялась желудочковой тахиаритмией — у 2 (25 %) пациентов. Наиболее тяжелая форма заболевания с выраженными клиническими проявлениями и эпизодом клинической смерти с последующими реанимационными мероприятиями, а также транзиторным удлинением интервала *QTc*, превышающим 500 мс, наблюдалось у пациентов с мутациями c.11814C > A (p.Ser3938Arg, rs794728704); c.463G > A (p.Gly155Arg) и c.14876G > A (p.Arg4959Gln, rs794728811) в гене *RYR2*. Имплантация кардиовертера-дефибриллятора потребовалась 3 (37,5 %) пациентам, в том числе 1 пациенту с целью первичной профилактики ВСС и 2 (25 %) — с целью вторичной профилактики.

Заключение. В настоящем исследовании изучен спектр клинических проявлений у пациентов с генетически подтвержденной КПЖТ. Транзиторное удлинение интервала *QTc*, выраженная синусовая брадикардия и суправентрикулярная тахиаритмия, сменяющиеся жизнеугрожающей желудочковой тахиаритмией с высокой частотой представлены у пациентов с КПЖТ.

Ключевые слова: катехоламинергическая полиморфная желудочковая тахикардия; мутации в гене *RYR2*; фенотипическое разнообразие.

Как цитировать

Комиссарова С.М, Ринейская Н.М., Чакова Н.Н., Ниязова С.С., Плащинская Л.И., Барсукевич В.Ч., Подпалова О.В. Клиническая и генетическая характеристика пациентов с катехоламинергической полиморфной желудочковой тахикардией (серия случаев) // Cardiac Arrhythmias. 2023. Т. 3, № 3. С. 27–40. DOI: https://doi.org/10.17816/cardar568180

Рукопись получена: 09.08.2023 **Рукопись одобрена:** 10.10.2023 **Опубликована:** 10.11.2023

ЭКО•ВЕКТОР

INTRODUCTION

Catecholaminergic polymorphic ventricular tachycardia (CPVT) is an inherited arrhythmic disorder characterized by bidirectional and/or polymorphic VT induced by physical or emotional stress [1]. In the absence of optimal therapy, the mortality rate of CPVT is extremely high, reaching 30%–50% by the age of 30 years [2]. The prevalence of CPVT is reported to be as high as 1:10,000; however, its true value remains unclear [3].

The molecular genetic cause of CPVT is a defect in the *RYR2* gene, located at 1q42, which encodes the cardiomyocyte ryanodine receptor 2, a major channel for calcium release from the sarcoplasmic reticulum (SR) [4]. *RYR2* gain-of-function mutations cause abnormal calcium release from the SR, resulting in delayed depolarization and ventricular arrhythmias observed in CPVT [5, 6]. In individuals with this pathology, 65% had mutations in the gene encoding the ryanodine receptor 2, which led to the development of CPVT type 1 (CPVT1). More recently, two studies have reported consanguineous families with CPVT whose members had homozygous missense and nonsense mutations in *CASQ2*, which encodes the SR-located Ca^{2+}-binding protein calsequestrin 2. CPVT caused by *CASQ2* mutations belongs to CPVT2, is characterized by autosomal recessive inheritance, and is much less common than CPVT1 [7, 8].

The main clinical manifestations of CPVT include syncope provoked by exercise, emotional stress, or administration of beta-adrenergic drugs. Noteworthily, approximately 30% of patients with CPVT were misdiagnosed with long *QT* syndrome (*LQTS*) by reason of the presence of transient *QT* prolongation > 460 ms [9].

The symptoms of CPVT with *QT* prolongation and *LQTS*, particularly with *LQTS* type 1, are similar in that physical activity causes ventricular arrhythmias that can result in sudden cardiac death (SCD). Accurate diagnosis is crucial for the reason that the incidence of arrhythmic events during beta-blocker therapy remains significantly higher in patients with CPVT than in those with LQTS [10]. Arrhythmias develop in patients with CPVT due to delayed depolarization caused by the large amounts of calcium released from the sarcoplasmic reticulum (SR), whereas patients with LQTS develop torsades de pointes (pirouette-type tachycardias) due to increased early post-depolarization and greater heterogeneity of monophasic duration between different myocardial sites resulting from impaired functioning of predominantly potassium channels.

Remarkably, sinus bradycardia, which is occasionally observed in patients with CPVT, may be another primary disorder caused by mutations associated with CPVT [11]. Moreover, sinus node dysfunction may paradoxically contribute to the initiation of ventricular rhythm disorders and may be therapeutically targeted to prevent exercise — or stress-induced ventricular arrhythmias in CPVT [12].

Patients with CPVT usually have a normal electrocardiogram (ECG) at rest. Nonetheless, the presence of sinus bradycardia in addition to a history of exercise- or emotion-induced cardiac symptoms may be critical to the diagnosis of CPVT before exercise testing [13]. Sinus bradycardia was reported in 5%–20% of patients who were carriers of a pathogenic *RYR2* mutation and who were identified by cascade screening (testing relatives for the presence of the mutation identified in the proband) [14]. Furthermore, supraventricular rhythm disorders other than sinus bradycardia (intermittent ectopic atrial rhythm, undefined supraventricular tachycardia (SVT), and sick sinus syndrome) were found in 16% of the total population (bradyarrhythmias in 11.3% and tachyarrhythmias in 4.7%) and 38% of those on Holter monitoring. Electrophysiological cardiac studies have confirmed that sinus node dysfunction is present in at least a subpopulation of patients with CPVT [15].

Several authors noted a polymorphism of rhythm disorders characteristic of patients with CPVT, including supraventricular and ventricular arrhythmias due to significant instability and the high proarrhythmogenic potential of the myocardium at all levels (both atrial and ventricular). Currently, CPVT is recognized as one of the major causes of SCD in young adults because of the high incidence of life-threatening arrhythmias.

This study aimed to present genetic and phenotypic characterization of probands and their family members for further evaluation of clinical features, including the development of adverse events and outcomes.

MATERIAL AND METHODS

Between 2019 and 2023, 8 patients diagnosed with CPVT (4 men and 4 women, median age 34 [31–41] years) from 6 unrelated families were followed up at the Republican Scientific and Practical Center "Cardiology."

Patients underwent regular inpatient examinations at least once a year (ECG–12, 24-hour Holter monitoring, implantable cardioverter defibrillator [ICD] monitoring), endocardial electrophysiological study (EEPS) as indicated, and collection of genealogical anamnesis with ECG evaluation of all family members in order to identify SCD cases or the presence of a familial disease. Structural myocardial abnormalities were excluded by echocardiographic study with the device IE-33 (Philips, USA) according to current recommendations [16].

Arrhythmic events were defined as the occurrence of syncope, sudden circulatory arrest, appropriate ICD therapy, and SCD. The control of arrhythmic events was assessed by ECG dynamics, 24-hour Holter monitoring,

and ICD monitoring throughout the follow-up period. ECG was performed on the Intekard-3 hardware–software complex (Republic of Belarus) by computer processing. ECG was monitored over 24 hours with the Oxford Medilog AR12 recorder (UK). ECG and 24-hour Holter monitoring were evaluated according to the classic standards of ECG diagnosis. ICD activation in response to the development of life-threatening ventricular arrhythmias — sustained pirouette-type VT or ventricular fibrillation (VF) — was considered appropriate. When an ICD was triggered for atrial fibrillation (AF) or other supraventricular arrhythmias, therapy was considered inappropriate. Supraventricular arrhythmias were defined as the presence of one and/or more of the following arrhythmias: atrioventricular nodal reentry tachycardia, ectopic atrial tachycardia, atrial fibrillation, and atrial flutter.

During diagnosis, all patients were prescribed beta-blockers: the drug of choice was propranolol at a dose of 40–80 mg in 2–3 doses, with a maximum dose of 320 mg/day. If ventricular arrhythmias were registered, propranolol was administered in maximum tolerated doses, and anamnesis of arrhythmic events was positive, drug therapy was continued with nadolol at a dose of at least 120–160 mg/day. If episodes of SVT were recorded in patients taking propranolol or nadolol, an antiarrhythmic drug of class IC or III was added to the basic antiarrhythmic therapy.

All probands underwent molecular genetic testing to verify the diagnosis and determine SCD risk. Mutations in the coding sequences of 174 genes associated with cardiovascular pathology, including CPVT, were searched by high-throughput sequencing on the NextSeq 550 Gene Analyzer (Illumina, USA) using the TruSight™ Cardio Panel (USA). The pathogenicity of new and previously described genetic variants was interpreted according to the 2015 recommendations of the American College of Medical Genetics and Genomics (ACMG) [17]. Pathogenic (class V), and likely pathogenic (class IV) genetic variants were considered clinically significant. Variants of uncertain clinical significance (VUS, class III pathogenicity) in genes associated with inherited arrhythmia were analyzed separately.

If pathogenicity class IV and V mutations were detected in the proband, the disclosed variant was confirmed by Sanger sequencing and cascade screening of the closest relatives.

RESULTS

Eight patients (4 men and 4 women) diagnosed with CPVT were followed up. Two of the patients were relatives of the probands. The median follow-up period (*Me* [*LQ; UQ*]) was 16 [9; 42] months.

Genotyping of patients revealed nucleotide sequence variants in *RYR2* of pathogenicity classes III–V according to the ACMG (2015) criteria: six class IV and V mutations and two VUS (class III) (Table 1).

In most cases (5 of 8 patients), more than 1 year had elapsed between manifestation and diagnosis. A familial disease form was present in 2 out of 6 probands (33.3%). Recurrent syncope episodes were registered in 3 (37.5 %) patients. At the time of diagnosis, bradycardia of < 54 beats per minute (bpm) was noted in 2 (25%) patients, and transient QT interval prolongation of > 480 ms was registered in 4 (50%) patients (Table 1).

By way of illustration, a 32-year-old female patient (mother of proband 13m) and her 8-year-old son (13m) had identical clinical manifestations, namely, syncope, short episodes of non-sustained VT with bradycardia, and episodes of exercise-unrelated transient *QTc* prolongation. The 8-year-old boy suddenly went into cardiac arrest with VF after emotional stress. Despite prolonged resuscitation and repeated cardioversions, clinical death was declared.

In the analysis of a series of ECGs available in the patient's outpatient chart, one of the 12-lead ECGs with sinus bradycardia at a heart rate of 54 bpm showed *QT* interval prolongation > 600 ms, repolarization abnormalities in the inferolateral leads, and T-pattern changes in leads V1–V2 (Fig. 1).

24-hour Holter ECG monitoring revealed premature ventricular contractions and episodes of non-sustained polymorphic VT (Fig. 2).

Genetic analysis of the proband revealed class IV likely pathogenic variant c.11814C > A (p.Ser3938Arg, rs794728704) in a heterozygous state in *RYR2* (Table 1).

The proband's mother experienced an increase in syncope episodes 13 months after her son's death. 24-hour Holter monitoring revealed polymorphic premature ventricular contractions (306 PVCs /day), PVC couplet, ventricular bigeminy, and 11 episodes of non-sustained polymorphic VT with an average heart rate of 170–179 bpm (Fig. 3). During wakefulness and sleep, 69 episodes of pathological *QTc* prolongation (⩾ 500 ms) with a total duration of 11 h 10 min (38 episodes during wakefulness and 31 episodes during night sleep) were recorded. The patient was prescribed the beta-blocker propranolol 40 mg ½ tablet three times/day; however, PVCs and episodes of non-sustained polymorphic VT persisted. The patient was tentatively diagnosed with transient LQTS based on clinical findings (SCD of her 8-year-old son and history of syncope), *QTc* prolongation of up to 600 ms on manual assessment of 24-hour Holter monitoring, and frequent episodes of non-sustained polymorphic VT. The Schwartz scale for LQTS was 5.0. An ICD was implanted for the primary prevention of SCD due to a high likelihood of recurrent arrhythmias. Appropriate ICD therapy during waking hours was recorded during regular follow-up visits.

Genetic testing of the mother revealed the same c.11814C > A mutation (p.Ser3938Arg, rs794728704) in a heterozygous state in *RYR2* as in the son. The diagnosis was altered, CPVT was established with transient abnormally prolonged *QT* and syncope episodes based on genotyping data, and ICD implantation was performed.

In a 28-year-old proband (code 763c) with recurrent syncope episodes, ECG-12 revealed marked sinus bradycardia with a heart rate of 45–50 bpm and QT prolongation up to 500 ms. 24-hour Holter monitoring revealed frequent PVCs (extrasystole index, 4.6%). The patient was prescribed propranolol at a dose of 40 mg three times a day and a pacemaker was implanted. Eight years later, the patient suffered from pacemaker lead infective endocarditis with a thrombus in the right atrium. The disease course was complicated by the development of a pulmonary

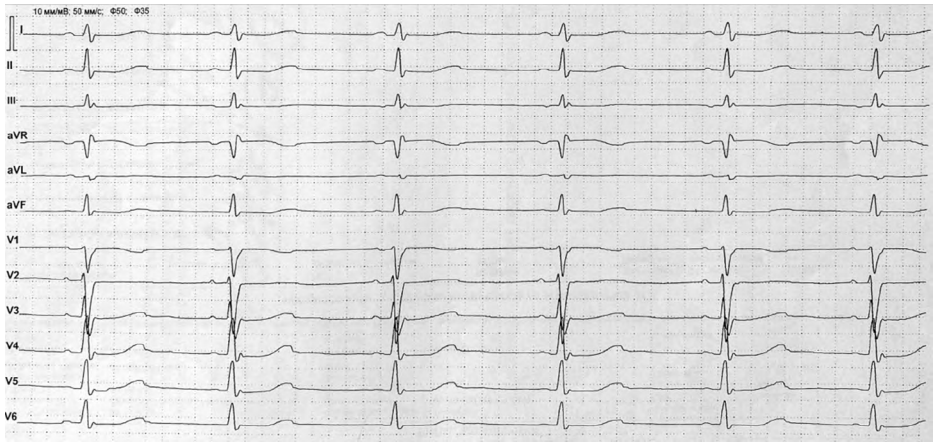
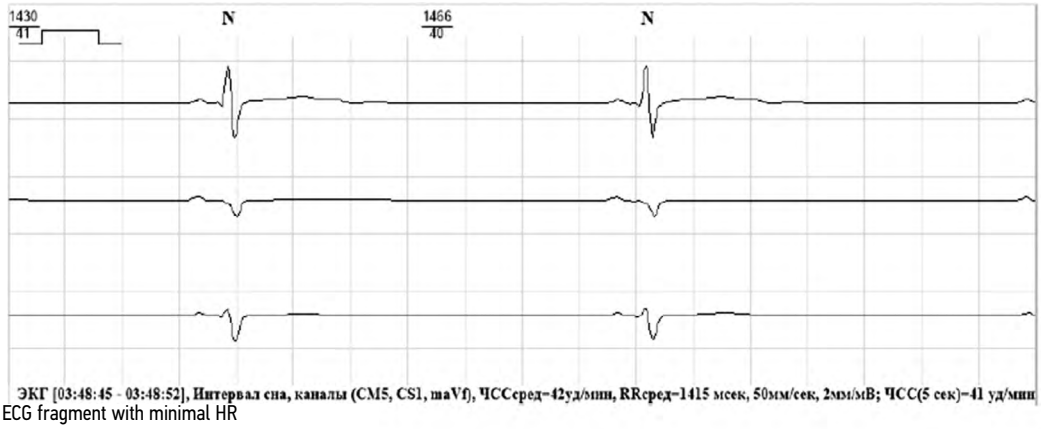
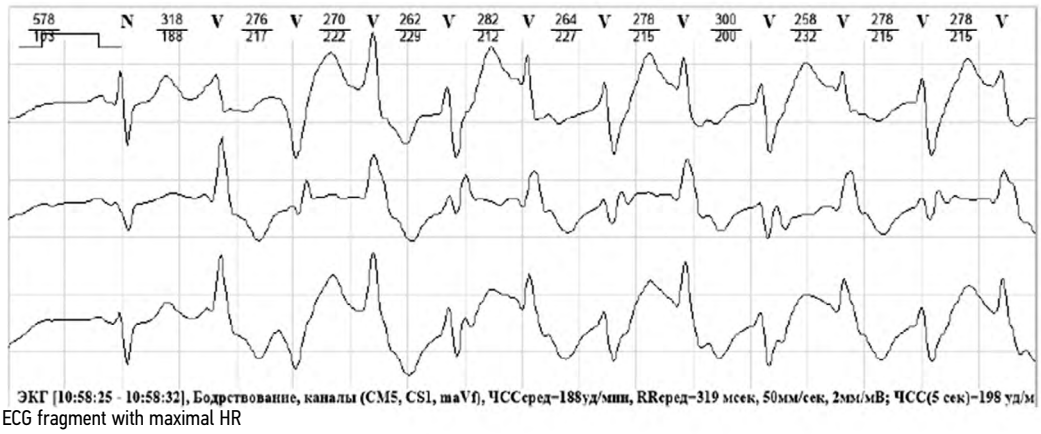


Fig. 1. Proband's 13m ECG-12
Рис. 1. Электрокрадиограмма в 12 отведениях пробанда 13м



ECG fragment with minimal HR



ECG fragment with maximal HR

Fig. 2. 24-hour holter monitoring of proband 13m ECG. Leads V5, II and aVF. ECG fragments with episodes of QTc prolongation up to 580 ms and nonsustained paroxysm of bidirectional VT
Рис. 2. Суточное мониторирование ЭКГ пробанда 13м. Отведения V5, II и aVF. Фрагменты ЭКГ с эпизодами удлинения *QTc* до 580 мс и неустойчивым пароксизмом двунаправленной ЖТ

Table 1. Clinical characterization of patients with mutations in the *RYR2* gene
Таблица 1. Клиническая характеристика пациентов с мутациями в гене *RYR2*

Patient code	Gender	Birth year	AC (amino acid) replacement, ID (dbSNP)	Pathogenicity class	Initial symptoms	Ventricular tachyarrhythmias	Atrial tachyarrhythmias	*QTc* interval, ms	EEPS with adrenergic stimulation, RFA	Therapy	Outcome
642s	Male	1996	p.Arg4959Gln, rs794728811	V	–	VF	–	500	–	Propranolol, ICD	Successful CPR, still on follow-up
Mother of 642s	Female	1978	p.Arg4959Gln, rs794728811	V	Asymptomatic	–	–	340	–	–	Asymptomatic, still on follow-up
13m	Male	2012	p.Ser3938Arg, rs794728704	IV	Frequent syncope episodes	Polymorphic VT/VF	–	600	–	–	Death
Mother of 13m	Female	1989	p.Ser3938Arg, rs794728704	IV	Frequent syncope episodes	Frequent PVCs polymorphic VT	–	500	–	Propranolol, ICD	Still on follow-up
763s	Female	1987	p.Gly155Arg, –	V	Frequent syncope episodes, bradycardia (heart rate, 45–48 bpm)	Frequent PVCs	–	500	EEPS (non-sustained paroxysm of VT was triggered)	Propranolol, pacemaker, ICD	Pacemaker lead infective endocarditis thrombus in the RA. PE
766s	Female	1989	p.Arg1086Ter, rs371303783	IV	–	Monomorphic VT	AVNRT with a heart rate of 170 bpm	350	EEPS RFA of slow-pathway AVNRT	Propranolol, propafenone, implantable loop recorder	Still on follow-up
833s	Male	1983	p.Thr1425Ala, rs776046135	VUS	–	Monomorphic sustained VT, polymorphic VT, VF	–	340	–	Propranolol	Still on follow-up
765s	Male	1877	p.Gly4315Glu, rs766109950	VUS	–	Sustained VT, polymorphic VT	Atrial flutter, AF	360	EEPS RFA of cavotricuspid isthmus. PV-cryo. RFA of VT	Propranolol, amiodarone, implantable loop recorder	Still on follow-up

Note: AC — amino acid; AF — atrial fibrillation; AVNRT — atrioventricular nodal reentrant tachycardia; CPR — cardiopulmonary resuscitation; EEPS — endocardial electrophysiologic study; ICD — implantable cardioverter defibrillator; PE — pulmonary artery thrombo embolism; PV-cryo — cryoballoon pulmonary vein isolation; RA — right atrium; RFA — radiofrequency ablation; PVCs — premature ventricular contractions; VF — ventricular fibrillation; VT — ventricular tachycardia.

Примечание: АК — аминокислота; ЭЭФИ — эндокардиальное электрофизиологическое исследование; РЧА — радиочастотная аблация; ФЖ — фибрилляция желудочков; ИКД — имплантируемый кардиовертер-дефибриллятор; СЛР — сердечно-легочная реанимация; ЖЭС — желудочковая экстрасистолия; ЖТ — желудочковая тахикардия; ЭКС — электрокардиостимулятор; ПП — правое предсердие; ТЭЛА — тромбоэмболия легочной артерии; ЧСС — частота сердечных сокращений; АВУРТ — атриовентрикулярная узловая реципрокная тахикардия; ТП — трепетание предсердий; ФП — фибрилляция предсердий; УЛВ — устья легочных вен.

DOI: https://doi.org/10.17816/cardar568180

embolism. Therefore, pacemaker lead extraction procedure and a 3D-modeled pulmonary artery thrombectomy were performed.

The genetic analysis a class V pathogenic variant c.463G > A (p.Gly155Arg) in a heterozygous state in *RYR2*, and the diagnosis was altered to CPVT. Despite medical treatment (propranolol at a dose of 160 mg), the patient had frequent PVCs and episodes of non-sustained polymorphic VT. During EEPS, a polymorphic VT paroxysm was provoked, and an ICD implantation was decided.

In one patient (code 642c), the disease manifested at the age of 15 years with the development of cardiovascular arrest and polymorphic VT/VF (Fig. 4), resuscitation was successful, and an ICD was implanted for the secondary prevention of SCD. In a series of ECGs preceding the arrhythmic event, *QT* prolongation of up to 500 ms was recorded. Genotyping revealed a pathogenic *RYR2* mutation c.14876G > A (p.Arg4959Gln, rs794728811). Based on the genotyping results, the patient was diagnosed with CPVT. The proband's mother had the same mutation, with clinical manifestations characterized by presyncope episodes and palpitations. Episodes of non-sustained VT were recorded during 24-hour Holter monitoring. Medical treatment (propranolol at a dose of 40 mg in 2–3 doses) was prescribed.

Episodes of SVT were reported in two patients (765c and 766c [25%]). Patient 765c was diagnosed with paroxysmal AF and atrial flutter and underwent EEPS, cryoballoon pulmonary vein isolation (PV-cryo), and radiofrequency ablation (RFA) of the inferior vena cava-tricuspid isthmus. Patient 766c was diagnosed with paroxysmal

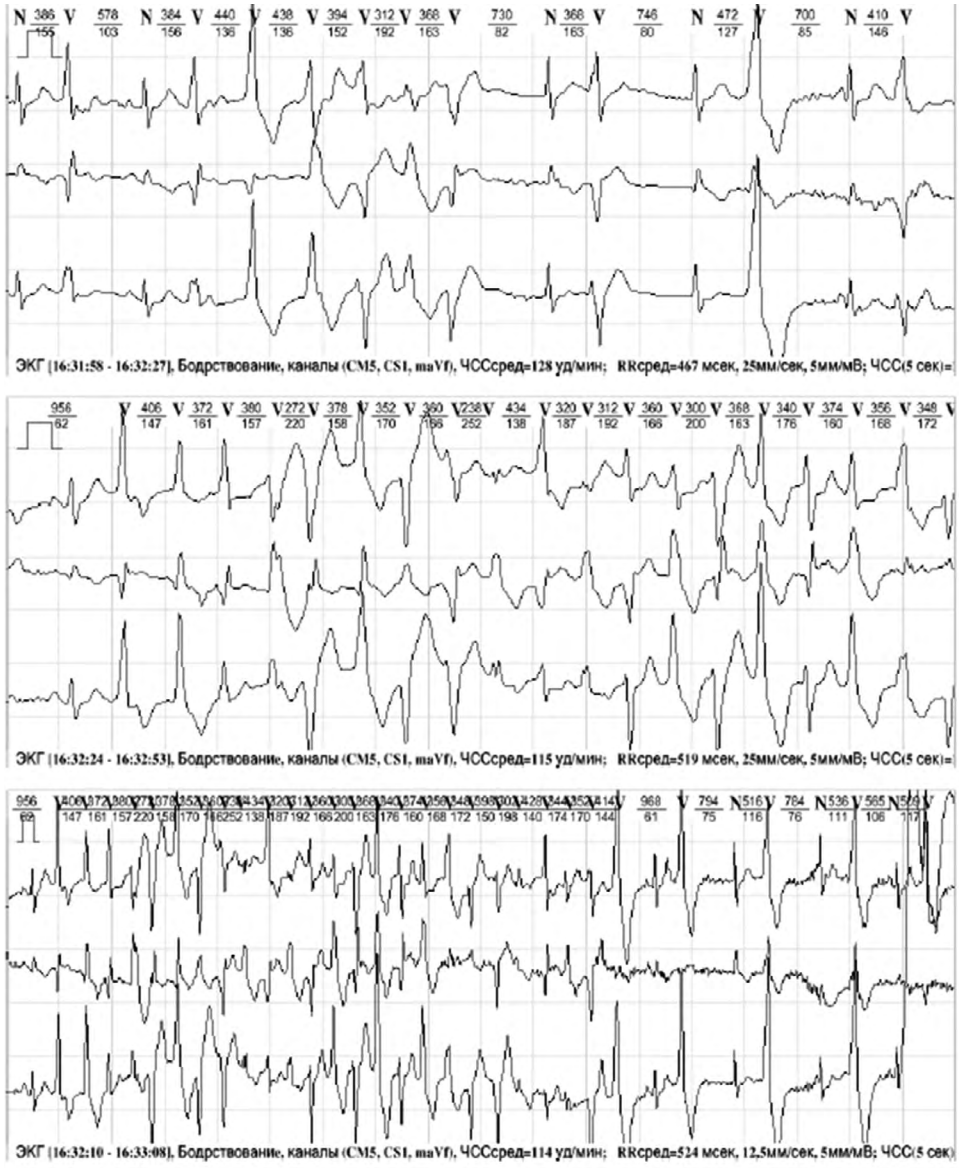


Fig. 3. 24-hour Holter monitoring of proband's 13m mother. Leads V5, II and aVF. ECG fragments with polymorphic PVCs and nonsustained VT paroxysm

Рис. 3. Суточное мониторирование ЭКГ матери пробанда 13м. Отведения V5, II и aVF. Фрагменты ЭКГ с полиморфной ЖЭС и неустойчивым пароксизмом ЖТ

atrioventricular nodal reentry tachycardia (AVNRT) and underwent EEPS and RFA of the slow pathways of the AV node. Genotyping of patients identified class III VUS in *RYR2*: c.12944G > A (p.Gly4315Glu, rs766109950) and c.3256C > T (p.Arg1086Ter, rs371303783).

In patient 815c, who had a novel likely pathogenic variant c.556G > T (p.Val186Leu, rs201211033) in *RYR2*, provocation of ventricular arrhythmias during EEPS with isoproterenol failed.

If arrhythmic events and/or recorded episodes of sustained polymorphic and/or bidirectional VT were present despite the medical therapy carried out, an ICD was implanted for secondary prevention of SCD. ATP therapy (Ramp) and appropriate ICD shocks were observed in 2 (25%) patients: patient 642c and the mother of proband 13m. Figs. 5–7 show an episode of sustained VT; after its detection, ATP therapy was sequenced twice (Ramp), and sinus rhythm was successfully restored.

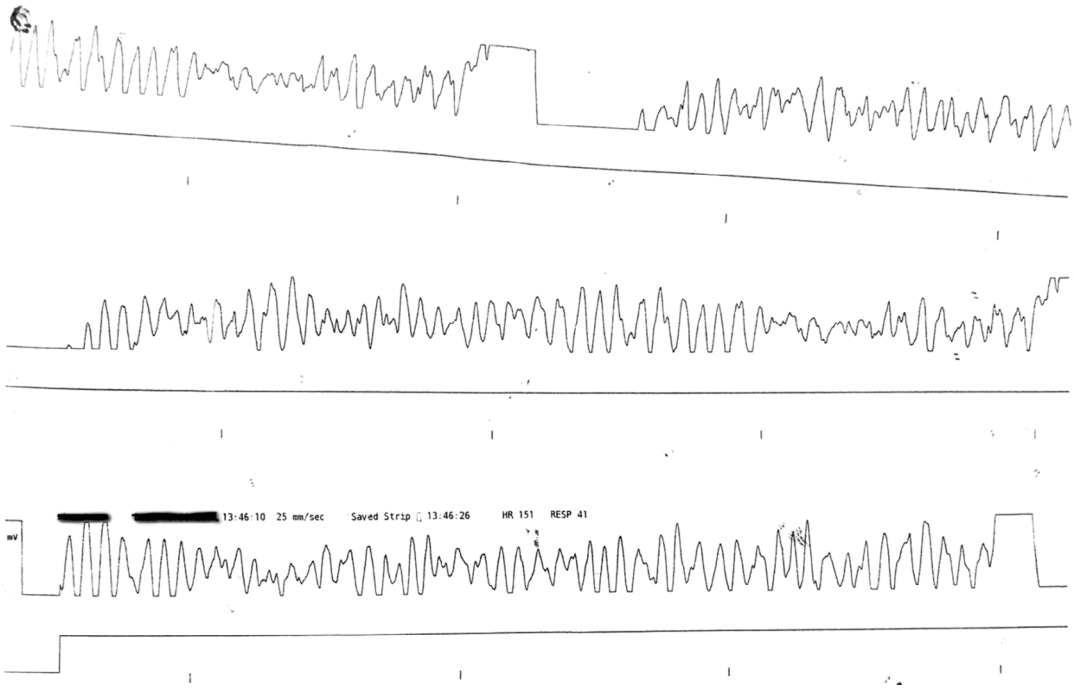


Fig. 4. ECG of patient 642c. ECG fragment with paroxysm of ventricular fibrillation
Рис. 4. ЭКГ пациента 642с. Фрагмент ЭКГ с пароксизмом крупноволновой ФЖ

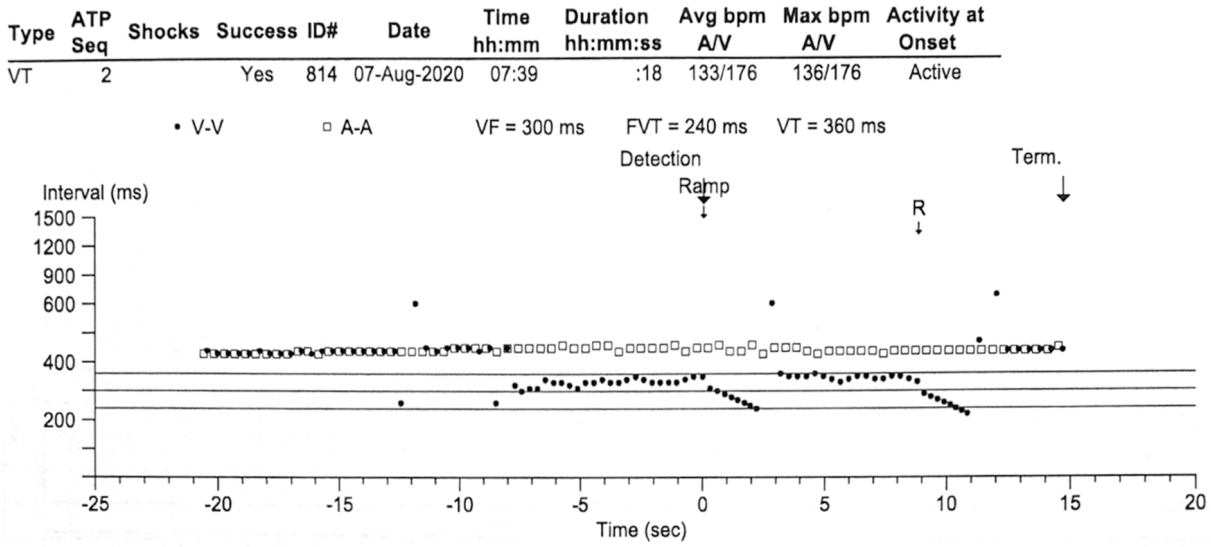


Fig. 5. The trend of ICD of proband's 13m mother representing episodes of sustained VT with ATP therapy
Рис. 5. Тренд ИКД матери пробанда 13м, представляющий эпизод устойчивой ЖТ с АТР-терапией

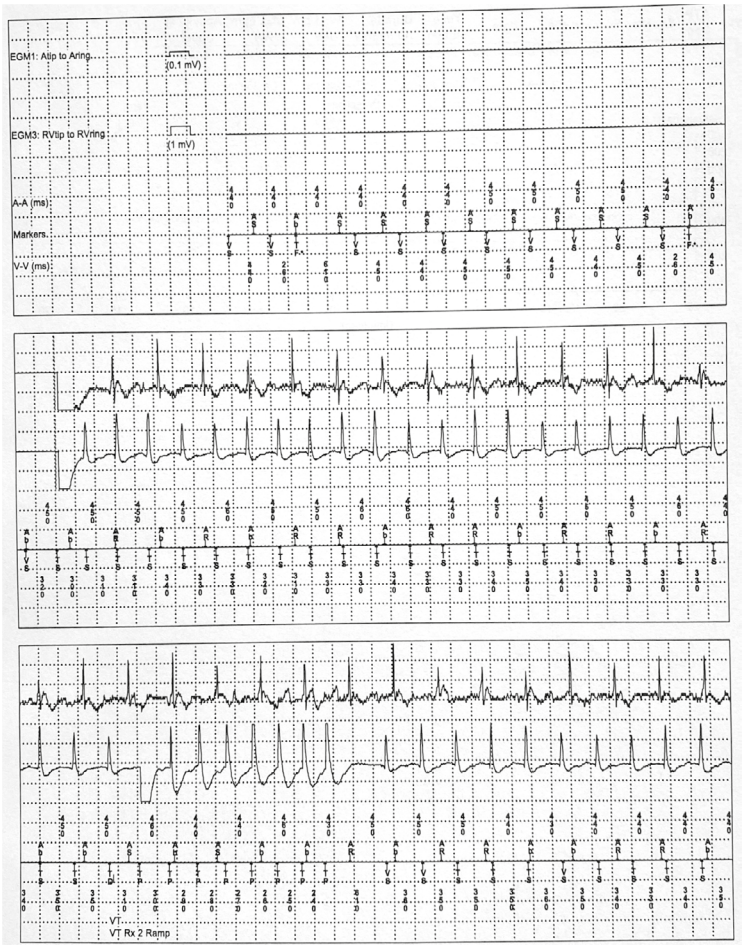


Fig. 6. Endogram fragment of proband's 13m mother representing the episode of sustained VT with the 1st attempt of Ramp ATP therapy (inefficient)
Рис. 6. Фрагмент эндограммы матери пробанда 13м, на которой представлен эпизод устойчивой ЖТ с 1-й попыткой АТР-терапии Ramp (безуспешной)

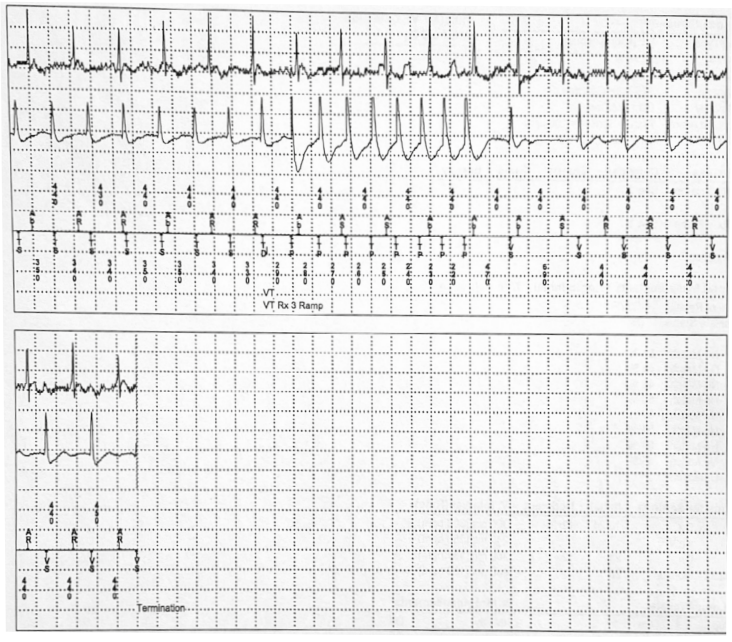


Fig. 7. Endogram fragment of proband's 13m mother representing the episode of sustained VT with the 2nd attempt of Ramp ATP therapy (efficient) and restoration of sinus rhythm
Рис. 7. Фрагмент эндограммы матери пробанда 13м, на которой представлен эпизод устойчивой ЖТ с 2-й попыткой АТР-терапии Ramp (успешной) и восстановлением синусового ритма

DISCUSSION

This study presented the clinical and genetic characteristics of eight patients with CPVT and *RYR2* mutations. The phenotypes of probands with CPVT shared common clinical manifestations: syncope episodes were usually triggered by physical activity or emotion, and in patient 642c, the disease manifested with cardiovascular arrest caused by VF at the age of 15 years. The median age of onset of CPVT symptoms in the observed probands (32 [28–41] years) is comparable to previously reported probands with *RYR2* mutations [18, 19]. However, some individuals with *RYR2* mutations may have a much later age of CPVT onset. In our study, 3 (37.5%) patients were asymptomatic until the age of 40 years. Various arrhythmias peculiar to CPVT were noted in the patients observed. To illustrate, the baseline resting ECG registered a transient prolonged *QTc* interval of up to 500 ms in 50% of the patients, and the majority had sinus bradycardia [20], as previously reported in non-genotyped populations [21, 22].

The fact that patients with CPVT and *RYR2* mutation exhibit significant bradycardia may help in the molecular diagnosis of (young) patients without structural heart diseases manifested by syncope events and slow heart rates but with normal *QTc* on resting ECG. For instance, a study of 29 non-genotyped Japanese patients of the same age with CPVT demonstrated sinus bradycardia [22]. This may be due to the presence of RYR2 channels in the functional SR of sinoatrial node cells, which serve as the main cardiac pacemakers [23]. Moreover, substances that impair SR function, such as ryanodine and cyclopiazonic acid, have negative chronotropic effects [23].

Thus, the bradycardia observed in carriers of *RYR2* mutations may be a direct implication of impaired Ca^{2+} regulation in sinoatrial node cells. However, this phenomenon may represent a vagus nerve feedback loop; a low mean heart rate reduces the likelihood of reaching the critical threshold of CPVT induction.

In this study, *QT* prolongation was observed in 50% of the patients with CPVT. Previous studies have demonstrated that certain CPVT cases were misdiagnosed as LQTS. Approximately 30% of patients with CPVT were misdiagnosed with LQTS in the presence of transient moderate *QT* prolongation of > 460 ms [9]. Tester et al. conveyed that nearly 6% of 269 patients with LQTS without mutations in genes associated with this pathology had *RYR2* mutations, which is primarily associated with CPVT [3]. Medeiros-Domingo et al. found that nearly one-third of patients with "atypical/probable" LQTS and exercise-induced syncope and *QT* with 480 ms had a missense *RYR2* mutation, indicating the need for differential diagnosis between LQTS and CPVT [10]. In a Japanese study by Ozawa et al [9], *RYR2* mutations were detected in 9 of 104 patients initially diagnosed with LQTS. They were misdiagnosed for four different reasons: (1) transient prolongation of the *QTc* after cardiopulmonary resuscitation, (2) prolongation of the *QTc* after epinephrine testing, (3) absence of ventricular arrhythmias on exercise testing, and (4) assumption of LQTS without evidence. CPVT-related ventricular arrhythmias can be reproduced during exercise testing or isoproterenol infusion. The induction of bidirectional VT establishes CPVT in the presence of a "borderline interval" of the *QTc*. Nevertheless, relatively few patients with *RYR2* mutations were reported to have an LQTS phenotype or an overlapping phenotype such as LQTS and CPVT [24].

The described clinical cases of patients with CPVT showed episodes of non-sustained polymorphic VT, unrelated to physical activity, against the background of bradycardia with episodes of transient *QTc* prolongation. In an 8-year-old proband, SCD resulted from polymorphic VT, which transformed into VF. The proband's mother (32 years old) had an ICD implanted for primary SCD prevention; hence, no exercise stress test could be performed. During follow-up, the *QTc* interval remained within the normal range; although, an appropriate ICD therapy for non-sustained polymorphic VT was recorded. Furthermore, in this study, CPVT episodes were not associated with physical activity and occurred at rest or under stress.

No international consensus diagnostic criteria exist to distinguish CPVT from LQTS, and definitive diagnosis is challenging in patients with both *QT* prolongation and polymorphic VT. Combined channelopathies with a phenotype of both CPVT and LQT may exist. For instance, Makita et al. [25] reported that two of five cases with mutations in the calmodulin gene showed overlapping signs of CPVT and LQTS. Further studies are needed to elucidate the causes of *QT* prolongation in patients with mutations in CPVT-associated genes.

Supraventricular arrhythmias such as AVNRT and AF, followed by ventricular arrhythmias, were recorded in 2 (25%) patients. Early active detection of supraventricular rhythm disorders in these patients is an additional tool of increasing the stress resistance of the ventricular myocardium and reducing the risk of ventricular arrhythmias.

Beta-blocker therapy in our patients had a generally favorable outcome, with seven of eight patients remaining asymptomatic at a mean follow-up of 6 years. Unfortunately, SCD occurred in one patient due to medical noncompliance following appropriate diagnosis and treatment. The doses of beta-blockers required to maintain the asymptomatic course of CPVT are higher than those used in LQTS [26].

ICDs were implanted in 4 (50%) patients who had polymorphic ventricular tachyarrhythmias during the stress testing (EEPS with epinephrine/isoproterenol) or 24-hour Holter monitoring.

The European Society of Cardiology Guidelines for the Management of Patients with Ventricular Arrhythmias and Prevention of Sudden Cardiac Death (ESC-2022) recommend ICD implantation in combination with beta-blockers and flecainide in patients with CPVT following an interrupted cardiac arrest (class I, level of evidence C). In addition, ICD implantation should be considered in patients with CPVT who have arrhythmogenic syncope and/or documented bidirectional/polymorphic VT while receiving the maximum tolerated dose of beta-blockers and flecainide (class IIa, level of evidence C) [27].

CONCLUSIONS

In summary, the clinical and genetic characteristics of patients with CPVT made it possible to evaluate clinical features, response to therapy, and genotype–phenotype correlation. Transient *QTc* prolongation, marked sinus bradycardia, and supraventricular tachyarrhythmias, followed by life-threatening ventricular tachyarrhythmias, are common in patients with CPVT and should be considered in the early diagnosis and selection of preventive strategies.

Limitations of the study

The study limitations include the relatively small number of patients due to the low incidence of the disease.

ADDITIONAL INFORMATION

Competing interests. The authors declare that they have no competing interests.

Funding source. This study was not supported by any external sources of funding.

ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Источник финансирования. Авторы заявляют об отсутствии внешнего финансирования при проведении исследования.

REFERENCES

1. Leenhardt A, Denjoy I, Guicheney P. Catecholaminergic polymorphic ventricular tachycardia. *Circ Arrhythm Electrophysiol*. 2012;5(5):1044–1052. DOI: 10.1161/CIRCEP.111.962027

2. Sumitomo N. Current topics in catecholaminergic polymorphic ventricular tachycardia. *J Arrhythmia*. 2016;32(5):344–351. DOI: 10.1016/j.joa.2015.09.008

3. Tester DJ, Kopplin LJ, Will ML, Ackerman MJ. Spectrum and prevalence of cardiac ryanodine receptor (RyR2) mutations in a cohort of unrelated patients referred explicitly for long QT syndrome genetic testing. *Heart Rhythm*. 2005;2(10):1099–10105. DOI: 10.1016/j.hrthm.2005.07.012

4. Marks AR. Ryanodine receptors/calcium release channels in heart failure and sudden cardiac death. *J Mol Cell Cardiol*. 2001;33(4):615–624. DOI: 10.1006/jmcc.2000

5. Priori SG, Napolitano C, Tiso N, et al. Mutations in the cardiac ryanodine receptor gene (hRyR2) underlie catecholaminergic polymorphic ventricular tachycardia. *Circulation*. 2001;103(2): 196–200. DOI: 10.1161/01.cir.103.2.196

6. Blayney LM, Lai FA. Ryanodine receptor-mediated arrhythmias and sudden cardiac death. *Pharmacol Ther*. 2009;123(2):151–177. DOI: 10.1016/j.pharmthera.2009.03.006

7. Lahat H, Pras E, Olender T, et al. A missense mutation in a highly conserved region of CASQ2 is associated with autosomal recessive catecholamine-induced polymorphic ventricular tachycardia in Bedouin families from Israel. *Am J Hum Genet*. 2001;69(6): 1378–1384. DOI: 10.1086/324565

8. Postma AV, Denjoy I, Hoorntje TM, et al. Absence of calsequestrin 2 causes severe forms of catecholaminergic polymorphic ventricular tachycardia. *Circ Res*. 2002;91(8):e21–26. DOI: 10.1161/01.res.0000038886.18992.6b

9. Ozawa J, Ohno S, Fujii Y, et al. Differential diagnosis between catecholaminergic polymorphic ventricular tachycardia and long QT syndrome type 1 – modified Schwartz score. *Circ J*. 2018;82(9): 2269–2276. DOI: 10.1253/circj.CJ-17-1032

10. Medeiros-Domingo A, Bhuiyan ZA, Tester DJ, et al. The RYR2-encoded ryanodine receptor/calcium release channel in patients diagnosed previously with either catecholaminergic polymorphic ventricular tachycardia or genotype negative, exercise-induced long QT syndrome: a comprehensive open reading frame mutational analysis. *J Am Coll Cardiol*. 2009;5(22):2065–2074. DOI: 10.1016/j.jacc.2009.08.022

11. Glukhov AV, Kalyanasundaram A, Lou Q, et al. Calsequestrin 2 deletion causes sinoatrial node dysfunction and atrial arrhythmias

associated with altered sarcoplasmic reticulum calcium cycling and degenerative fibrosis within the mouse atrial pacemaker complex1. *Eur Heart J*. 2015;36(11):686–697. DOI: 10.1093/eurheartj/eht452

12. Faggioni M, Hwang HS, van der Werf C, et al. Accelerated sinus rhythm prevents catecholaminergic polymorphic ventricular tachycardia in mice and in patients. *Circ Res*. 2013;112(4):689–697. DOI: 10.1161/CIRCRESAHA.111.300076

13. Postma AV, Denjoy I, Kamblock J, et al. Catecholaminergic polymorphic ventricular tachycardia: RYR2 mutations, bradycardia, and follow up of the patients. *J Med Genet*. 2005;42(11):863–870. DOI: 10.1136/jmg.2004.028993

14. van der Werf C, Nederend I, Hofman N, et al. Familial evaluation in catecholaminergic polymorphic ventricular tachycardia: disease penetrance and expression in cardiac ryanodine receptor mutation-carrying relatives. *Circ Arrhythm Electrophysiol*. 2012;5(4):748–756. DOI: 10.1161/CIRCEP.112.970517

15. Sumitomo N, Sakurada H, Taniguchi K, et al. Association of atrial arrhythmia and sinus node dysfunction in patients with catecholaminergic polymorphic ventricular tachycardia. *Circ J*. 2007;71(10):1606–1609. DOI: 10.1253/circj.71.1606

16. Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr*. 2015;28(1):1–39.e14. DOI: 10.1016/j.echo.2014.10.003

17. Richards S, Aziz N, Bale S, et al. Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. *Genet Med*. 2015;17(5):405–424. DOI: 10.1038/gim.2015.30

18. Priori SG, Napolitano C, Memmi M, et al. Clinical and molecular characterization of patients with catecholaminergic polymorphic ventricular tachycardia. *Circulation*. 2002;106(1):69–74. DOI: 10.1161/01.cir.0000020013.73106.d8

19. Choi G, Kopplin LJ, Tester DJ, et al. Spectrum and frequency of cardiac channel defects in swimming-triggered arrhythmia syndromes. *Circulation*. 2004;11(15):2119–2124. DOI: 10.1161/01.CIR.0000144471.98080.CA

20. Rijnbeek PR, Witsenburg M, Schrama E, et al. New normal limits for the paediatric electrocardiogram. *Eur Heart J*. 2001;22(8):702–711. DOI: 10.1053/euhj.2000.2399

21. Leenhardt A, Lucet V, Denjoy I, et al. Catecholaminergic polymorphic ventricular tachycardia in children. A 7-year follow-up of 21 patients. *Circulation*. 1995;91(5):1512–1519. DOI: 10.1161/01.cir.91.5.1512

22. Sumitomo N, Harada K, Nagashima M, et al. Catecholaminergic polymorphic ventricular tachycardia: electrocardiographic characteristics and optimal therapeutic strategies to prevent sudden death. *Heart*. 2003;89(1):66–70. DOI: 10.1136/heart.89.1.66

23. Rigg L, Heath BM, Cui Y, Terrar DA. Localisation and functional significance of ryanodine receptors during beta-adrenoceptor stimulation in the guinea-pig sino-atrial node. *Cardiovasc Res*. 2000;48(2):254–264. DOI: 10.1016/s0008-6363(00)00153-x

24. Shigemizu D, Aiba T, Nakagawa H, et al. Exome analyses of long QT syndrome reveal candidate pathogenic mutations in calmodulin-interacting genes. *PLoS One*. 2015;10(7):e0130329. DOI: 10.1371/journal.pone.0130329

25. Makita N, Yagihara N, Crotti L, et al. Novel calmodulin mutations associated with congenital arrhythmia susceptibility. *Circ Cardiovasc Genet*. 2014;7(4):466–474. DOI: 10.1161/CIRCGENETICS.113.000459

26. Ackerman MJ, Priori SG, Dubin AM, et al. Beta-blocker therapy for long QT syndrome and catecholaminergic polymorphic ventricular tachycardia: Are all beta-blockers equivalent? *Heart Rhythm*. 2017;14(1):e41–e44. DOI: 10.1016/j.hrthm.2016.09.012

27. Zeppenfeld K, Tfelt-Hansen J, de Riva M, et al. 2022 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death. *Eur Heart J*. 2022;43(40):3997–4126. DOI: 10.1093/eurheartj/ehac262

СПИСОК ЛИТЕРАТУРЫ

1. Leenhardt A., Denjoy I., Guicheney P. Catecholaminergic polymorphic ventricular tachycardia // Circ Arrhythm Electrophysiol. 2012. Vol. 5, No. 5. P. 1044–1052. DOI: 10.1161/CIRCEP.111.962027

2. Sumitomo N. Current topics in catecholaminergic polymorphic ventricular tachycardia // J Arrhythmia. 2016. Vol. 32, No. 5. P. 344–351. DOI: 10.1016/j.joa.2015.09.008

3. Tester D.J., Kopplin L.J., Will M.L., Ackerman M.J. Spectrum and prevalence of cardiac ryanodine receptor (RyR2) mutations in a cohort of unrelated patients referred explicitly for long QT syndrome genetic testing // Heart Rhythm. 2005. Vol. 2, No. 10. P. 1099–10105. DOI: 10.1016/j.hrthm.2005.07.012

4. Marks A.R. Ryanodine receptors/calcium release channels in heart failure and sudden cardiac death // J Mol Cell Cardiol. 2001. Vol. 33, No. 4. P. 615–624. DOI: 10.1006/jmcc.2000

5. Priori S.G., Napolitano C., Tiso N., et al. Mutations in the cardiac ryanodine receptor gene (hRyR2) underlie catecholaminergic polymorphic ventricular tachycardia // Circulation. 2001. Vol. 103, No. 2. P. 196–200. DOI: 10.1161/01.cir.103.2.196

6. Blayney L.M., Lai F.A. Ryanodine receptor-mediated arrhythmias and sudden cardiac death // Pharmacol Ther. 2009. Vol. 123, No. 2. P. 151–177. DOI: 10.1016/j.pharmthera.2009.03.006

7. Lahat H., Pras E., Olender T., et al. A missense mutation in a highly conserved region of CASQ2 is associated with autosomal recessive catecholamine-induced polymorphic ventricular tachycardia in Bedouin families from Israel // Am J Hum Genet. 2001. Vol. 69, No. 6. P. 1378–1384. DOI: 10.1086/324565

8. Postma A.V., Denjoy I., Hoorntje T.M., et al. Absence of calsequestrin 2 causes severe forms of catecholaminergic polymorphic ventricular tachycardia // Circ Res. 2002. Vol. 91, No. 8. P. e21–26. DOI: 10.1161/01.res.0000038886.18992.6b

9. Ozawa J., Ohno S., Fujii Y., et al. Differential diagnosis between catecholaminergic polymorphic ventricular tachycardia and long QT syndrome type 1 – modified Schwartz score // Circ J. 2018. Vol. 82, No. 9. P. 2269–2276. DOI: 10.1253/circj.CJ-17-1032

10. Medeiros-Domingo A., Bhuiyan Z.A., Tester D.J., et al. The RYR2-encoded ryanodine receptor/calcium release channel in patients diagnosed previously with either catecholaminergic polymorphic ventricular tachycardia or genotype negative, exercise-induced long QT syndrome: a comprehensive open reading frame mutational analysis // J Am Coll Cardiol. 2009. Vol. 5, No. 22. P. 2065–2074. DOI: 10.1016/j.jacc.2009.08.022

11. Glukhov A.V., Kalyanasundaram A., Lou Q., et al. Calsequestrin 2 deletion causes sinoatrial node dysfunction and atrial arrhythmias associated with altered sarcoplasmic reticulum calcium cycling and degenerative fibrosis within the mouse atrial pacemaker complex1 // Eur Heart J. 2015. Vol. 36, No. 11. P. 686–697. DOI: 10.1093/eurheartj/eht452

12. Faggioni M., Hwang H.S., van der Werf C., et al. Accelerated sinus rhythm prevents catecholaminergic polymorphic ventricular tachycardia in mice and in patients // Circ Res. 2013. Vol. 112, No. 4. P. 689–697. DOI: 10.1161/CIRCRESAHA.111.300076

13. Postma A.V., Denjoy I., Kamblock J., et al. Catecholaminergic polymorphic ventricular tachycardia: RYR2 mutations, bradycardia, and follow up of the patients // J Med Genet. 2005. Vol. 42, No. 11. P. 863–870. DOI: 10.1136/jmg.2004.028993

14. van der Werf C., Nederend I., Hofman N., et al. Familial evaluation in catecholaminergic polymorphic ventricular tachycardia: disease penetrance and expression in cardiac ryanodine receptor mutation-carrying relatives // Circ Arrhythm Electrophysiol. 2012. Vol. 5, No. 4. P. 748–756. DOI: 10.1161/CIRCEP.112.970517

15. Sumitomo N., Sakurada H., Taniguchi K., et al. Association of atrial arrhythmia and sinus node dysfunction in patients with catecholaminergic polymorphic ventricular tachycardia // Circ J. 2007. Vol. 71, No. 10. P. 1606–1609. DOI: 10.1253/circj.71.1606

16. Lang R.M., Badano L.P., Mor-Avi V., et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging // J Am Soc Echocardiogr. 2015. Vol. 28, No. 1. P. 1–39.e14. DOI: 10.1016/j.echo.2014.10.003

17. Richards S., Aziz N., Bale S., et al. Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology // Genet Med. 2015. Vol. 17, No. 5. P. 405–424. DOI: 10.1038/gim.2015.30

18. Priori S.G., Napolitano C., Memmi M., et al. Clinical and molecular characterization of patients with catecholaminergic polymorphic ventricular tachycardia // Circulation. 2002. Vol. 106, No. 1. P. 69–74. DOI: 10.1161/01.cir.0000020013.73106.d8

19. Choi G., Kopplin L.J., Tester D.J., et al. Spectrum and frequency of cardiac channel defects in swimming-triggered arrhythmia syndromes // Circulation. 2004. Vol. 11, No. 15. P. 2119–2124. DOI: 10.1161/01.CIR.0000144471.98080.CA

20. Rijnbeek P.R., Witsenburg M., Schrama E., et al. New normal limits for the paediatric electrocardiogram // Eur Heart J. 2001. Vol. 22, No. 8. P. 702–711. DOI: 10.1053/euhj.2000.2399

21. Leenhardt A., Lucet V., Denjoy I., et al. Catecholaminergic polymorphic ventricular tachycardia in children. A 7-year follow-up of 21 patients // Circulation. 1995. Vol. 91, No. 5. P. 1512–1519. DOI: 10.1161/01.cir.91.5.1512

22. Sumitomo N., Harada K., Nagashima M., et al. Catecholaminergic polymorphic ventricular tachycardia: electrocardiographic characteristics and optimal therapeutic strategies to prevent sudden death // Heart. 2003. Vol. 89, No. 1. P. 66–70. DOI: 10.1136/heart.89.1.66

23. Rigg L., Heath B.M., Cui Y., Terrar D.A. Localisation and functional significance of ryanodine receptors during beta-adrenoceptor stimulation in the guinea-pig sino-atrial node // Cardiovasc Res. 2000. Vol. 48, No. 2. P. 254–264. DOI: 10.1016/s0008-6363(00)00153-x

24. Shigemizu D., Aiba T., Nakagawa H., et al. Exome analyses of long QT syndrome reveal candidate pathogenic mutations in calmodulin-interacting genes // PLoS One. 2015. Vol. 10, No. 7. ID e0130329. DOI: 10.1371/journal.pone.0130329

25. Makita N., Yagihara N., Crotti L., et al. Novel calmodulin mutations associated with congenital arrhythmia susceptibility // Circ Cardiovasc Genet. 2014. Vol. 7. No. 4. P. 466–474. DOI: 10.1161/CIRCGENETICS.113.000459

26. Ackerman M.J., Priori S.G., Dubin A.M., et al. Beta-blocker therapy for long QT syndrome and catecholaminergic polymorphic ventricular tachycardia: Are all beta-blockers equivalent? // Heart Rhythm. 2017. Vol. 14, No. 1. P. e41–e44. DOI: 10.1016/j.hrthm.2016.09.012

27. Zeppenfeld K., Tfelt-Hansen J., de Riva M., et al. 2022 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death // Eur Heart J. 2022. Vol. 43, No. 40. P. 3997–4126. DOI: 10.1093/eurheartj/ehac262

ОБ АВТОРАХ

***Надежда Михайловна Ринейская,** канд. мед. наук, младший научный сотрудник лаборатории хронической сердечной недостаточности ГУ «РНПЦ „Кардиология"»; ORCID: 0000-0002-1986-1367; eLibrary SPIN: 2782-2270; e-mail: nadya.rin@gmail.com

Светлана Михайловна Комиссарова, д-р мед. наук, доцент, главный научный сотрудник лаборатории хронической сердечной недостаточности ГУ «РНПЦ «Кардиология»; ORCID: 0000-0001-9917-5932; eLibrary SPIN: 8023-5308; e-mail: kom_svet@mail.ru

Наталья Николаевна Чакова, канд. биол. наук, ведущий научный сотрудник лаборатории генетики животных ГНУ «Институт генетики и цитологии НАН Беларуси»; ORCID: 0000-0003-4721-9109; eLibrary SPIN: 5682-1497; e-mail: chaknat@mail.ru

Светлана Сергеевна Ниязова, младший научный сотрудник лаборатории генетики животных ГНУ «Институт генетики и цитологии НАН Беларуси»; ORCID: 0000-0002-3566-7644; eLibrary SPIN: 1093-1793; e-mail: kruglenko_sveta@tut.by

Лариса Иосифовна Плащинская, канд. мед. наук, ведущий научный сотрудник лаборатории нарушений сердечного ритма ГУ «РНПЦ «Кардиология»; ORCID: 0000-0001-8815-3543; eLibrary SPIN: 2666-1270; e-mail: lario2001@mail.ru

Вероника Чеславовна Барсукевич, канд. мед. наук, ведущий научный сотрудник лаборатории нарушений сердечного ритма ГУ «РНПЦ «Кардиология»; ORCID: 0000-0002-5180-7950; eLibrary SPIN: 9413-7121; e-mail: barsukevich.v@gmail.com

Ольга Владиславовна Подпалова, канд. мед. наук, научный сотрудник лаборатории нарушений сердечного ритма ГУ «РНПЦ «Кардиология»; ORCID: 0000-0002-7162-3737; eLibrary SPIN: 1617-8500; e-mail: olgapodpalova22@gmail.com

AUTHORS INFO

***Nadiia M. Rineiska,** Cand. Sci. (Med.), junior researcher, Laboratory of Chronic Heart Failure, State Institution Republican Scientific and Practical Centre "Cardiology"; ORCID: 0000-0002-1986-1367; eLibrary SPIN: 2782-2270; e-mail: nadya.rin@gmail.com

Svetlana M. Komissarova, MD, Dr. Sci. (Med.), Associate Professor, chief researcher, Laboratory of Chronic Heart Failure, State Institution Republican Scientific and Practical Centre "Cardiology"; ORCID: 0000-0001-9917-5932; eLibrary SPIN: 8023-5308, e-mail: kom_svet@mail.ru

Natalya N. Chakova, Cand. Sci. (Biol.), PhD, leading researcher, Laboratory of Animal Genetics, Institute of Genetics and Cytology of Belarus National Academy of Sciences; ORCID: 0000-0003-4721-9109; eLibrary SPIN: 5682-1497; e-mail: chaknat@mail.ru

Svetlana N. Niyazova, junior researcher, Laboratory of Animal Genetics, Institute of Genetics and Cytology of Belarus National Academy of Sciences; ORCID: 0000-0002-3566-7644; eLibrary SPIN: 1093-1793; e-mail: kruglenko_sveta@tut.by

Larisa I. Plashchinskaya, Cand. Sci. (Med.), leading researcher, Laboratory of Cardiac Arrhythmias, State Institution Republican Scientific and Practical Centre "Cardiology"; ORCID: 0000-0001-8815-3543; eLibrary SPIN: 2666-1270; e-mail: lario2001@mail.ru

Veronika Ch. Barsukevich, Cand. Sci. (Med.), leading researcher, Laboratory of Cardiac Arrhythmias, State Institution Republican Scientific and Practical Centre "Cardiology"; ORCID: 0000-0002-5180-7950; eLibrary SPIN: 9413-7121; e-mail: barsukevich.v@gmail.com

Olga V. Podpalova, Cand. Sci. (Med.), researcher, Laboratory of Cardiac Arrhythmias, State Institution Republican Scientific and Practical Centre "Cardiology"; ORCID: 0000-0002-7162-3737; eLibrary SPIN: 1617-8500; e-mail: olgapodpalova22@gmail.com

* Автор, ответственный за переписку / Corresponding author

DOI: https://doi.org/10.17816/cardar567837

Review article

European guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death 2022: cardiomyopathy. What's new?

Tatiana N. Novikova, Fatima I. Bitakova, Valeria S. Ignateva, Vladimir I. Novikov, Sergey A. Sayganov, Vladislava A. Shcherbakova

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

Abstract

The review provides information on new indications that should be guiden the diagnosis and treatment of ventricular arrhythmias in patients with cardiomyopathy. The analysis of modern definitions and classifications of cardiomyopathy is given. The issues of ventricular arrhythmias in different cardiomyopathy phenotypes, risk stratification of sudden cardiac death and its prevention are considered in detail.

Keywords: ventricular arrhythmias; sudden cardiac death; dilated cardiomyopathy; hypertrophic cardiomyopathy; arrhythmogenic cardiomyopathy; restrictive cardiomyopathy; non-compaction cardiomyopathy.

To cite this article

Novikova TN, Bitakova FI, Ignateva VS, Novikov VI, Sayganov SA, Shcherbakova VA. European guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death 2022: cardiomyopathy. What's new? *Cardiac Arrhythmias.* 2023;3(3):41–62. DOI: https://doi.org/10.17816/cardar567837

Received: 29.07.2023 **Accepted:** 27.10.2023 **Published:** 10.11.2023

DOI: https://doi.org/10.17816/cardar567837

Обзорная статья

Европейские рекомендации по лечению пациентов с желудочковыми аритмиями и профилактике внезапной сердечной смерти 2022 года: кардиомиопатии. Что нового?

Т.Н. Новикова, Ф.И. Битакова, В.С. Игнатьева, В.И. Новиков, С.А. Сайганов, В.А. Щербакова

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

Аннотация

В обзоре представлена информация о новых показаниях, которыми следует руководствоваться при диагностике и лечении желудочковых нарушений ритма у пациентов с кардиомиопатиями. Дан анализ современных определений и классификаций кардиомиопатий. Подробно рассмотрены вопросы желудочковых нарушений ритма при разных фенотипах кардиомиопатий, стратификации риска внезапной сердечной смерти и ее профилактики.

Ключевые слова: желудочковые аритмии; внезапная сердечная смерть; дилатационная кардиомиопатия; гипертрофическая кардиомиопатия; аритмогенная кардиомиопатия; рестриктивная кардиомиопатия; некомпактный миокард желудочков.

Как цитировать

Новикова Т.Н., Битакова Ф.И., Игнатьева В.С., Новиков В.И., Сайганов С.А., Щербакова В.А. Европейские рекомендации по лечению пациентов с желудочковыми аритмиями и профилактике внезапной сердечной смерти 2022 года: кардиомиопатии. Что нового? // Cardiac Arrhythmias. 2023. Т. 3, № 3. С. 41–62. DOI: https://doi.org/10.17816/cardar567837

Рукопись получена: 29.07.2023 **Рукопись одобрена:** 27.10.2023 **Опубликована:** 10.11.2023

In the new European recommendations for treating patients with ventricular arrhythmias (VAs), a large section is devoted to cardiomyopathies (CMPs). Cardiac arrhythmias are perhaps one of the key clinical symptoms of these relatively rare diseases, and sudden cardiac death (SCD) is the classic complication of most CMPs.

This section focuses on CMPs in the order they are presented in European recommendations.

Dilated cardiomyopathy (DCM)

DCM is characterized by dilatation and systolic dysfunction of the left ventricle or both ventricles and is not associated with ischemic heart disease (IHD) or abnormal hemodynamic loads (such as arterial hypertension and valvular disease) [1, 2]. SCD occurs in 12% of patients with DCM and accounts for 25%–35% of the overall cause of death in DCM [3–5].

According to the literature, DCM affects 1 per 2500–2700 populations [6, 7]. However, the true incidence is most likely higher.

The causes of the appearance of DCM in a patient can be genetic, acquired, or mixed when a genetic predisposition is formed in the presence of external factors, for example, the pre- and postpartum period, alcohol abuse, chemotherapy, and others [8]. Pathogenic mutations are detected in 25–55% of patients with DCM, with a predominant autosomal dominant type of inheritance [2]. More often than others, mutations are found in the titin (*TTN*) (31%) and lamin (*LMNA*) (14.3%) genes [9]. Mutations in genes such as *LMNA, PLN* (encodes the phospholamban protein), *RBM20* (encodes the splicing transcription factor), and *FLNC* (encodes filamin C) are associated with a high risk of VAs and SCD [10–14]. Carriers of desmosomal and *LMNA* mutations have a high incidence of VAs and SCD, which does not depend on the LV ejection fraction (EF) [14]. The identification of pathogenic mutations plays an important role in SCD risk stratification.

The phenotype, particularly in a genetically determined disease, upon disease onset may not correspond to the standard criteria for the disease and may change over time. Thus, in the early disease stages, the patient may only have a decrease in EF without dilatation of the cardiac chambers. In this regard, a new category of DCM has been proposed, that is, hypokinetic nondilated cardiomyopathy (HNDCM) [8]. HNDCM is characterized by LV or biventricular global systolic dysfunction (LVEF <45%) without dilatation, and systolic dysfunction is not associated with abnormal myocardial stress or coronary artery disease [8]. The 2023 European guidelines for the management of patients with CMPs made a special attention to this syndrome. It has been proposed to initially replace the term "hypokinetic nondilated cardiomyopathy" with "nondilated left ventricular cardiomyopathy" (NDLVCMP) and then to identify NDLVCMP as a new independent phenotype of CMPs [15]. The term "NDLVCM" introduced in 2023 appears to be a broader concept than HNDCM. NDLVCMP is characterized by the presence of LV nonischemic scarring or fatty degeneration, regardless of the presence or absence of global or local impairment of wall mobility or isolated global hypokinesia of the LV walls without scarring. This disease is also characterized by ventricular rhythm disturbances.

An integrated approach to diagnosing DCM is essential. The role of echocardiography (EchoCG), particularly in the early disease stages, is undeniable. Magnetic resonance imaging (MRI) of the heart with contrast enhancement enables not only to determine LVEF but also to identify areas of fibrosis and, by their localization, clarify the etiology (ischemic, i.e., subendocardial, transmural fibrosis, corresponding in localization to the blood supply system of a certain coronary artery; nonischemic, i.e., diffuse interstitial intramural, subepicardial fibrosis, or subendocardial, but not corresponding to the blood supply system of a particular coronary artery) [16, 17]. In addition, MRI findings, along with genetic data, can contribute to SCD risk stratification [2]. According to a meta-analysis of 29 studies that pooled MRI findings from 2,948 patients with DCM, late gadolinium enhancement (LGE) is associated with an increased risk of arrhythmic endpoints (VA and SCD), major cardiovascular events, and all-cause death [18]. A recent study of 1020 patients with DCM revealed that both LGE and LVEF were risk markers for all-cause and cardiovascular deaths; however, only LGE was associated with the risk of SCD [19]. The recommendations emphasize the importance of performing cardiac MRI with contrast in patients with DCM/HNDCM.

The registration of electrocardiograms (ECG) is recommended not only for patients but also for their first-degree relatives. The presence of pathology of the sinus and atrioventricular (AV) nodes, most often in combination with bundle branch blocks, when the disease manifests at a young age should raise suspicion of *LMNA*-associated DCM with a poor prognosis [20].

The recommendations for genetic testing are presented in Table 1 [2].

The recommendations for examining patients and their relatives are presented in Table 2 [2].

The 2022 European guidelines provide an algorithm for risk stratification and primary prevention of sudden cardiac death in patients with DCM/HNDCM (Fig. 1) [2].

Given the high risk of SCD, patients with DCM need not only secondary but also primary prevention of SCD. The 2022 European guidelines provide clear guidance on who is eligible for primary and secondary prevention of SCD. Because the main clinical manifestation of DCM/HNDCM is chronic heart failure (CHF), treatment of CHF, in accordance with current recommendations,

is mandatory for at least 3 months before deciding on implantable cardioverter-defibrillator (ICD) implantation for the primary prevention of SCD [2]. The patient's cardiac function and clinical status after 3 months of optimal medical therapy (OMT) must be re-evaluated before the initial prophylactic implantation of an ICD. LVEF with OMT can be significantly improved in DCM caused by myocarditis or TTN mutations [2].

The recommendations for the primary prevention of SCD are presented in Table 3 [2].

The recommendations for the secondary prevention of sudden cardiac death are presented in Table 4 [2].

ICDs reduce the risk of not only arrhythmic death but also death from all causes [2]. Moreover, frequent, painful ICD shocks worsen the quality of life of the patients. The implantation of ICDs with antitachycardia pacing (ATP)

Table 1. Recommendations for genetic testing for dilated/hypokinetic nondilated cardiomyopathy
Таблица 1. Рекомендации по генетическому тестированию при дилатационной / гипокинетической недилатационной кардиомиопатии

Recommendation	Indication class	Evidence level
Genetic testing including at least the *LMNA*, *PLN*, *RBM20*, and *FLNC* genes is recommended for patients with DCM/HNDCM and – disorders of atrioventricular conduction under the age of 50 years; or – with a family history of DCM/HNDCM or cases of sudden cardiac death in a first-degree relative (aged < 50 years)	I	B
Genetic testing including at least the *LMNA*, *PLN*, *RBM20*, and *FLNC* genes should be recommended for risk stratification in patients with overt sporadic DCM/HNDCM diagnosed at a young age or when the patient has signs suggestive of a hereditary etiology of the disease	IIa	C

Note: DCM — dilated cardiomyopathy; HNDCM — hypokinetic nondilated cardiomyopathy; *LMNA* — nuclear lamin gene; *PLN* — phospholamban gene, *RBM20* — gene encoding a splicing transcription factor; *FLNC* — filamin C gene.

Примечание: ДКМП — дилатационная кардиомиопатия; ГНДКМП — гипокинетическая недилатационная кардиомиопатия; *LMNA* — ген ядерных ламинов; *PLN* — ген фосфоламбана, *RBM20* — ген, кодирующий транскрипционный фактор сплайсинга; *FLNC* — ген филамина С.

Table 2. Recommendations for the examination of patients suffering from dilated/hypokinetic non-dilated cardiomyopathy and their relatives
Таблица 2. Рекомендации по обследованию пациентов, страдающих дилатационной / гипокинетической недилатационной кардиомиопатией, и их родственников

Recommendation	Indication class	Evidence level
Cardiac MRI with late gadolinium enhancement should be recommended in patients with DCM/HNDCM to evaluate the etiology and risk of ventricular arrhythmia/SCD.	IIa	B
In patients with DCM/HNDCM, electrophysiological testing should be recommended if there is a history of syncope, and the cause remains unexplained after noninvasive evaluation.	IIa	B
First-degree relatives of patients with DCM/HNDCM are advised to undergo an ECG and echocardiogram if – the diagnosis was established in an index patient aged < 50 years or clinical signs indicating a hereditary cause of the disease are present; or – the presence of DCM/HNDCM or premature SCD in the family history	I	C
An ECG and echocardiogram may be recommended for first-degree relatives of patients with apparently sporadic DCM/HNDCM	IIb	C

Note: SCD — sudden cardiac death; DCM — dilated cardiomyopathy; HNDCM — hypokinetic nondilated cardiomyopathy; MRI — magnetic resonance imaging.

Примечание: ВСС — внезапная сердечная смерть; ДКМП — дилатационная кардиомиопатия; ГНДКМП — гипокинетическая недилатационная кардиомиопатия; МРТ — магнитно-резонансная томография.

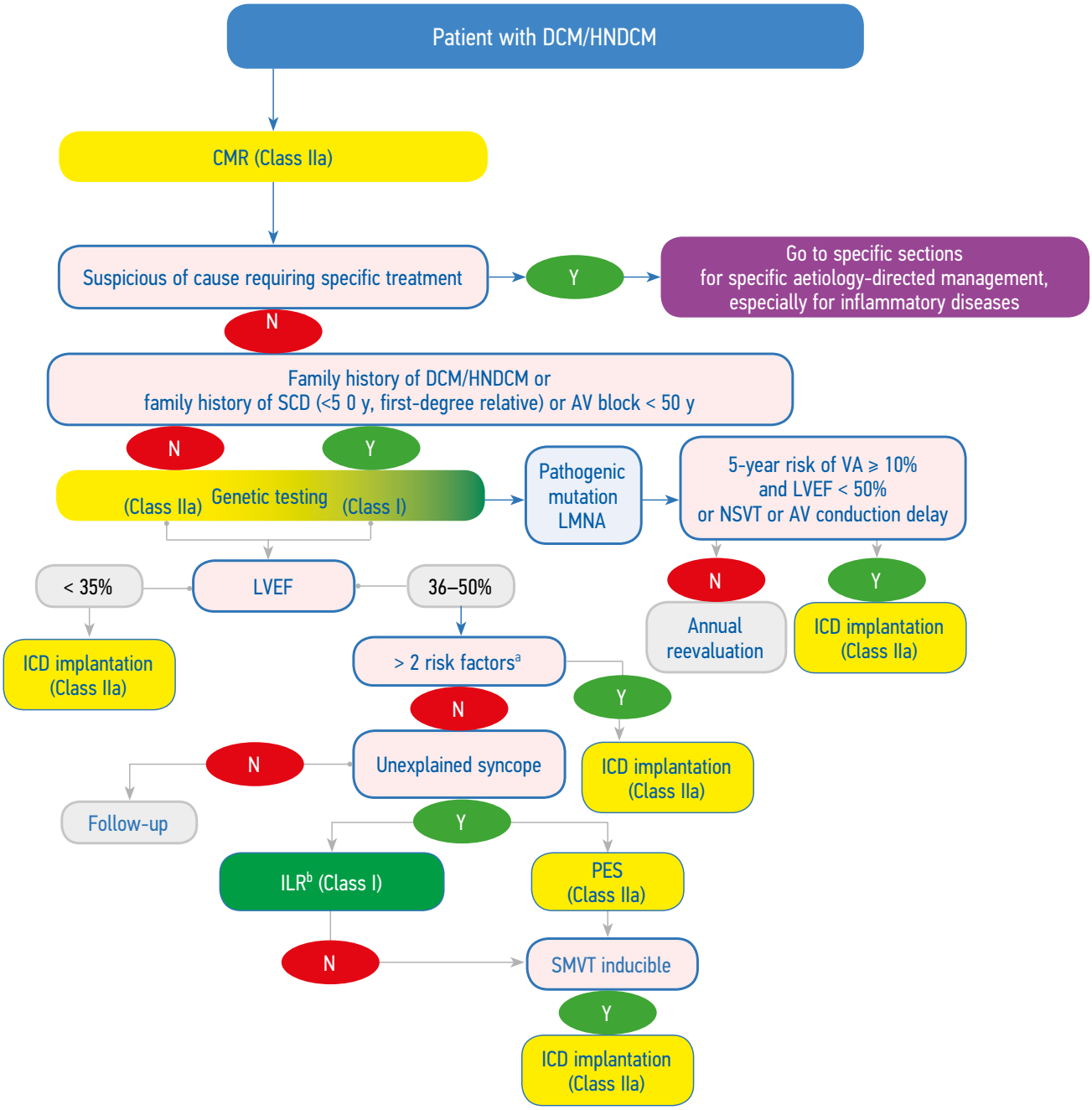


Fig. 1. Algorithm for risk stratification and primary prevention of sudden cardiac death in patients with dilated cardiomyopathy/hypokinetic non-dilated cardiomyopathy [2]

AV — atrioventricular; CMR — cardiac magnetic resonance; DCM — dilated cardiomyopathy; HNDCM — hypokinetic non-dilated cardiomyopathy; ICD — implantable cardioverter defibrillator; ILR — implantable loop recorder; LMNA — nuclear lamin gene; LVEF — left ventricular ejection fraction; N — no; NSVT — non-sustained ventricular tachycardia; PES, programmed electrical stimulation; SCD — sudden cardiac death; SMVT — sustained monomorphic ventricular tachycardia; VA — ventricular arrhythmias; Y — yes

[a] Risk factors: unexplained syncope, pathogenic variants in PLN, FLNC, or RBM20, LGE on CMR, inducible SMVT at PES. [b] The 2018 ESC Guidelines for the diagnosis and management of syncope

Рис. 1. Алгоритм стратификации риска и первичной профилактики внезапной сердечной смерти у пациентов с дилатационной кардиомиопатией / гипокинетической недилатационной кардиомиопатией [2].

АВ — атриовентрикулярная; ВСС — внезапная сердечная смерть; ДКМП — дилатационная кардиомиопатия; ГНДКМП — гипокинетическая недилатационная кардиомиопатия; ЖА — желудочковые аритмии; ИПР — имплантируемые петлевые регистраторы; ИКД — имплантируемый кардиовертер-дефибриллятор; ЛЖ — левый желудочек; МРТ — магнитно-резонансная томография; НУЖТ — неустойчива желудочковая тахикардия; УМЖТ — устойчивая мономорфная желудочковая тахикардия; ФВ — фракция выброса; ЭФИ — электрофизиологическое исследование; *LMNA* — ген ядерных ламинов

[a] Обмороки, фиброз при МРТ сердца, индуцируемые устойчивые мономорфные желудочковые тахикардии при эндоЭФИ, патогенные мутации в *LMNA*, *PLN*, *FLNC* и генах *RBM20*. [b] Согласно рекомендациям ESC 2018 года по диагностике и лечению обмороков

Таблица 3. Рекомендации по первичной профилактике внезапной сердечной смерти у пациентов, страдающих дилатационной / гипокинетической недилатационной кардиомиопатией
Table 3. Recommendations for the primary prevention of sudden cardiac death in patients suffering from dilated/hypokinetic nondilated cardiomyopathy

Recommendation	Indication class	Evidence level
ICD implantation should be recommended in patients with DCM/HNDCM, symptomatic heart failure (NYHA classes II–III), and LVEF ⩽35% after ⩾3 months of OMT	IIa	A
ICD implantation should be recommended for patients with DCM/HNDCM who have a pathogenic *LMNA* mutation if the estimated 5-year risk of life-threatening ventricular arrhythmias is ⩾10% and in the following cases: – unstable ventricular tachycardia; or – LVEF <50%; or – disorders of AV conduction	IIa	B
ICD implantation should be recommended for patients with DCM/HNDCM, LVEF <50%, and presence of ⩾2 risk factors: – syncope – late gadolinium enhancement in cardiac MRI – inducible sustained monomorphic ventricular tachycardia with endoEPS (electrophysiological study) – pathogenic *LMNA*, *PLN*, *FLNC*, and *RBM20* mutations	IIa	C

Note: AV — atrioventricular; CMR — cardiac magnetic resonance; DCM — dilated cardiomyopathy; HNDCM — hypokinetic non-dilated cardiomyopathy; EF — ejection fraction; ICD — implantable cardioverter defibrillator; LV, left ventricul; NYHA, New York Heart Association; LMNA — nuclear lamin gene; PES — programmed electrical stimulation; PLN — phospholamban gene; RBM20 — gene encoding a splicing transcription factor; FLNC — filamin C gene. [a] Based on the risk calculator LMNA-risk VTA calculator Risk Prediction Score for Life-Threatening Ventricular Tachyarrhythmias in Laminopathies (https://lmna-risk-vta.fr/).

Примечание: АВ — атриовентрикулярное; ДКМП — дилатационная кардиомиопатия; ГНДКМП — гипокинетическая недилатационная кардиомиопатия; ИКД — имплантируемый кардиовертер-дефибриллятор; ЛЖ — левый желудочек; МРТ — магнитно-резонансная томография; ОМТ — оптимальная медикаментозная терапия; ФВ — фракция выброса; ЭФИ — электрофизиологическое исследование; NYHA — New York Heart Association; *LMNA* — ген ядерных ламинов; *PLN* — ген фосфоламбана, *RBM20* — ген, кодирующий транскрипционный фактор сплайсинга; *FLNC* — ген филамина С. [a] Риск рассчитывается с помощью калькулятора LMNA-risk VTA calculator Risk Prediction Score for Life-Threatening Ventricular Tachyarrhythmias in Laminopathies (https://lmna-risk-vta.fr/)

Таблица 4. Рекомендации по вторичной профилактике внезапной сердечной смерти у пациентов, страдающих дилатационной / гипокинетической недилатационной кардиомиопатией
Table 4. Recommendations for secondary prevention of sudden cardiac death in patients suffering from dilated/hypokinetic nondilated cardiomyopathy

Recommendation	Indication class	Evidence level
ICD implantation is recommended for patients with DCM/HNDCM who have experienced sudden circulation arrest due to ventricular tachycardia/ventricular fibrillation or hemodynamically intolerable sustained monomorphic ventricular tachycardia	I	B
Catheter ablation in specialized centers should be recommended for patients with DCM/HNDCM and recurrent, symptomatic, sustained monomorphic ventricular tachycardia, frequent ICD shocks for sustained monomorphic ventricular tachycardia, and if antiarrhythmic drugs are ineffective, contraindicated, or intolerant	IIa	C
The addition of amiodarone orally or substitution of a beta blocker with sotalol should be recommended in patients with DCM/HNDCM and ICD who experience recurrent, symptomatic ventricular arrhythmias despite optimal device programing and beta-blocker treatment	IIa	B
ICD implantation is recommended in patients with DCM/HNDCM and hemodynamically tolerated sustained monomorphic ventricular tachycardia	IIa	C

Note: DCM — dilated cardiomyopathy; HNDCM — hypokinetic nondilated cardiomyopathy; ICD — implantable cardioverter defibrillator.

Примечание: ДКМП — дилатационная кардиомиопатия; ГНДКМП — гипокинетическая недилатационная кардиомиопатия; ИКД — имплантируемый кардиовертер-дефибриллятор.

functionality and optimization of ICD programing can reduce the number of ICD shocks delivered in response to ventricular tachycardia (VT); however, additional drug therapy is almost always required to reduce symptomatic episodes of VA [2]. The recommendations for antiarrhythmic drug selection are based on the results of the OPTIC trial, where 412 patients with ICD within 21 days after VT/ventricular fibrillation (VF) were randomized to three antiarrhythmic treatment groups: amiodarone plus beta-blocker, sotalol alone, or beta-blocker alone. The frequency of ICD shocks after 1 year was 10.3% in the amiodarone and beta-blocker group, 24.3% in the sotalol group, and 38.5% in the beta-blocker group [21]. Only limited data are available on the efficiency and safety of sodium channel blockers in reducing the number of ICD activations in DCM [2]. They may be useful for reducing VAs only in a few patients without severe heart failure and low LVEF. The recommendations emphasize the need to align the level of efficiency and drug-related side effects when choosing antiarrhythmic therapy.

In DCM, monomorphic VTs predominate (Fig. 2), which are based on the reentry mechanism.

To reduce the number of monomorphic VTs, catheter ablation can be used in addition to drug therapy. However, the rate of recurrent VTs after catheterization procedures in patients with DCM is higher than that in patients with IHD, the VT-free survival 1 year after a catheter procedure in DCM is 40.5%, whereas in IHD, it is 57% [22]. Some patients require repeated procedures, after which the probability of the absence of recurrence of arrhythmia increases. When the arrhythmic focus is subepicardial, epicardial ablation is required in

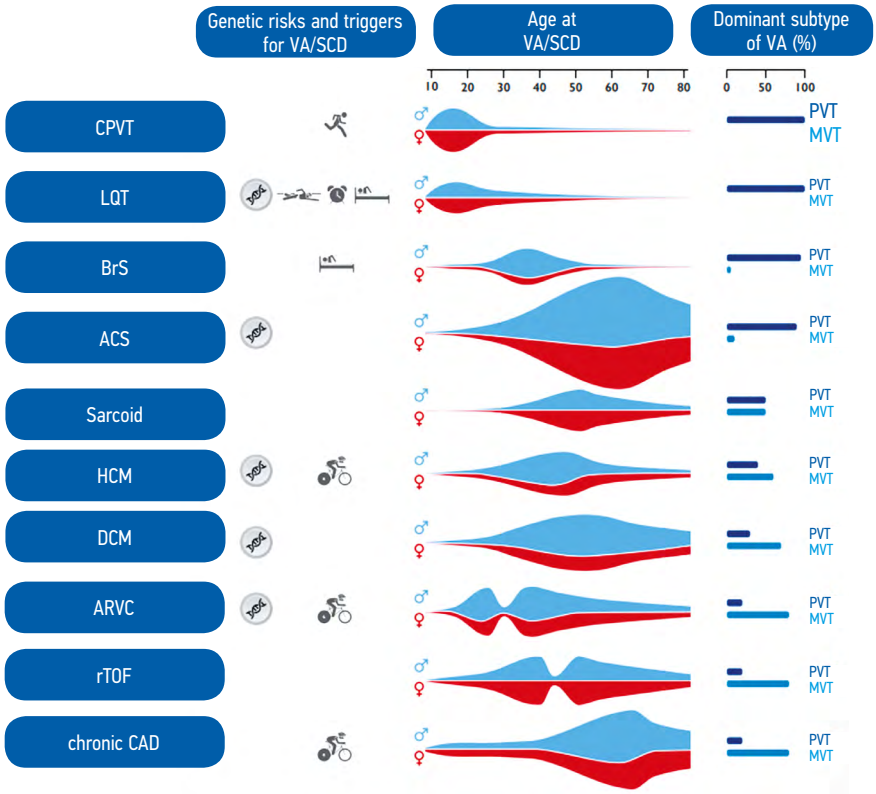


Fig. 2. Genetic risk for VA/SCD, typical triggers for VA/SCD, age at presentation with VA/SCD, sex predominance, and typical VA in different diseases associated with VA/SCD

— presence of genetic risks; — trigger — physical and emotional stress; — trigger — swimming, diving; — syncope during sleep; —trigger — a sharp sound; — trigger – physical stress

ACS — acute coronary syndrome; ARVC — arrhythmogenic right ventricular cardiomyopathy; BrS — Brugada syndrome; CAD — coronary artery disease; CPVT — catecholaminergic polymorphic ventricular tachycardia; DCM — dilated cardiomyopathy; HCM — hypertrophic cardiomyopathy; LQT — long QT syndrome; MVT — monomorphic ventricular tachycardia; PVT — polymorphic ventricular tachycardia; rTOF — repaired tetralogy of Fallot; SCD — sudden cardiac death; VA — ventricular arrhythmia

Рис. 2. Генетический риск желудочковой аритмии / внезапной сердечной смерти, типичные триггеры желудочковой аритмии / внезапной сердечной смерти, возраст при появлении желудочковой аритмии / внезапной сердечной смерти, преобладание пола и вариант типичной желудочковой аритмии при различных заболеваниях, связанных с желудочковой аритмией / внезапной сердечной смертью [2]

— наличие генетических рисков; — триггер — физическая и эмоциональная нагрузки; — триггер — плавание, ныряние; — синкопальные состояния во сне; — триггер — резкий звук; — триггер — физическая нагрузка

ВСС — внезапная сердечная смерть; ЖА — желудочковые аритмии; МЖТ — мономорфная желудочковая тахикардия; ПЖТ — полиморфная желудочковая тахикардия

Table 5. General recommendations for patients with mutations in genes encoding lamin
Таблица 5. Общие рекомендации для пациентов с мутацией генов, кодирующих синтез ламинов

Recommendation	Indication class	Evidence level
Patients with DCM/HNDCM and the *LMNA* mutation are not recommended to participate in high-intensity training, including competitive sports	III	C

Note: DCM — dilated cardiomyopathy; HNDCM — hypokinetic nondilated cardiomyopathy; *LMNA* — nuclear lamin gene.
Примечание: ДКМП — дилатационная кардиомиопатия; ГНДКМП — гипокинетическая недилатационная кардиомиопатия; *LMNA* — ген ядерных ламинов.

27%–30% of the procedures [22, 23]. The outcome is particularly poor in patients with pathogenic *LMNA* mutations. Because of the deep transmural, anteroseptal location of the substrate, transcoronary ethanol ablation, bipolar ablation, and surgical ablation may be required [24–26].

The general recommendations for patients with *LMNA* mutations are presented in Table 5.

Arrhythmogenic right ventricular cardiomyopathy (ACM)

ACM is characterized by the replacement of the myocardium with fibrous and fatty tissue [27]. Currently, it is more correct to talk about ACM of both ventricles [28]. The prevalence of ACM in the population ranges from 1:1000 to 1:5000 [29]. Most often, ACM is caused by pathogenic mutations in desmosomal genes (*Dsc2,* desmocollin-2; *Dsg2,* desmoglein-2; *Dsp,* desmoplakin; *Pkg,* plakoglobin; *Pkp2*, plakophilin-2) and less often in nondesmosomal genes. Similar to DCM, in ACM, some mutations are associated with a high risk of developing VA at a young age [30, 31]. The diagnosis of ACM is complex and requires searching and assessing certain criteria. Although the recommendations contain a reference in Guidelines 2022 to the publication of Corrado et al. (2020) [28], the criteria for diagnosing ACM are not the 2020 Padua criteria but the previous 2010 criteria [32]. As an advantage, the Padua criteria provide an algorithm for diagnosing not only the right ventricular but also the LV process. Figure 3 presents the ECG of our 16-year-old patient with arrhythmogenic cardiomyopathy. ECG was performed during sinus rhythm. At the beginning of the recording, the moment of the cessation of unstable polymorphic VT (three complexes) was recorded. In addition, frequent polymorphic single and paired premature ventricular complexes (PVC) of the bigeminy type were noted. The major Padua criterion for the diagnosis of right ventricular ACM was identified, namely, inverted *T* waves in right precordial

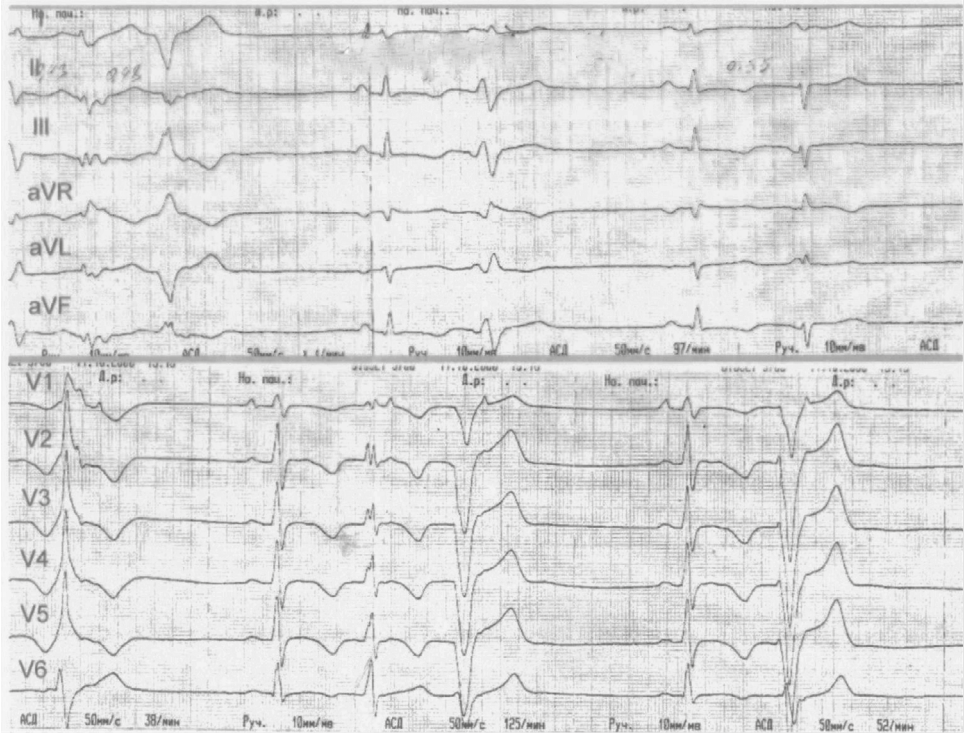


Fig. 3. Electrocardiogram of a patient suffering from biventricular arrhythmogenic cardiomyopathy (explanation in the text)
Рис. 3. Электрокардиограмма пациента, страдающего бивентрикулярной аритмогенной кардиомиопатией (объяснение в тексте)

leads V1, V2, and V3 in a patient with complete pubertal development, and the absence of complete right bundle branch block. In addition, minor Padua criteria were noted for the diagnosis of LV ACM, which are inverted *T* waves in left precordial leads *V4–V6* in the absence of complete left bundle branch (LBB) block and low-amplitude *QRS* (< 0.5 mV peak-to-peak) in the limb leads to the absence of obesity, emphysema, and pericardial effusion.

Figure 4 presents the ECG of one of the patients with right ventricular ACM during classical sustained VT, which is a major criteria for diagnosing right ventricular ACM — VT with QRS morphology similar to LBB block, causing the deviation of the electrical axis to the left upward (not from the right ventricle (RV) outflow tract, the focus is located in the area of the RV free wall).

During the natural disease course in patients with ACM who have not been implanted with ICD, cardiac arrest occurs in 4.6%–6.1% of cases [33–36]. Because of the high incidence of VA and SCD in ACM, risk stratification of adverse arrhythmic events is required. In 16%–19% of cases, the indication for ICD is rapid VT (⩾ 250 beats/min) or VF, which are considered surrogate markers of a potentially life-threatening event [37–40]. Recently, a risk model was developed to predict any persistent VA in ACM based on the analysis of the disease course of 528 patients with an established diagnosis of ACM and no history of VA. During model development, age, sex, arrhythmic syncope, nonsustained VT, number of ventricular PVC, number of leads with *T*-wave inversion, and RV EF (c-index 0.77) were collected [41]. Another model for predicting life-threatening VA was proposed based on the analysis of 864 patients with ACM, which included male sex, age, number of ventricular PVC within 24 h, and number of leads with *T*-wave inversion (c-index 0.74) as predictors [41]. However, validation studies are required before these risk models can be recommended for clinical use [2].

The recommendations for the diagnostics and management of patients with arrhythmogenic cardiomyopathy are presented in Table 6 [2].

The recommendations for the risk stratification and primary prevention of SCD are presented in Table 7 [2].

RV and LV dysfunctions are associated with high arrhythmic risk. The guidelines state that EF thresholds for indications for ICD implantation are difficult to define; however, even asymptomatic patients with severe RV dysfunction (right ventricular area fraction change ⩽ 17% or RV EF ⩽ 35%) should be advised to implant an ICD for the primary prevention of SCD. Similarly, patients with ACM with significant LV disease (LVEF ⩽ 35%) are candidates for ICD implantation according to current ICD guidelines for DCM [2]. An ICD for the primary prevention of SCD should also be recommended in patients with symptomatic ACM (presyncope or palpitations suggestive of VA) and moderate

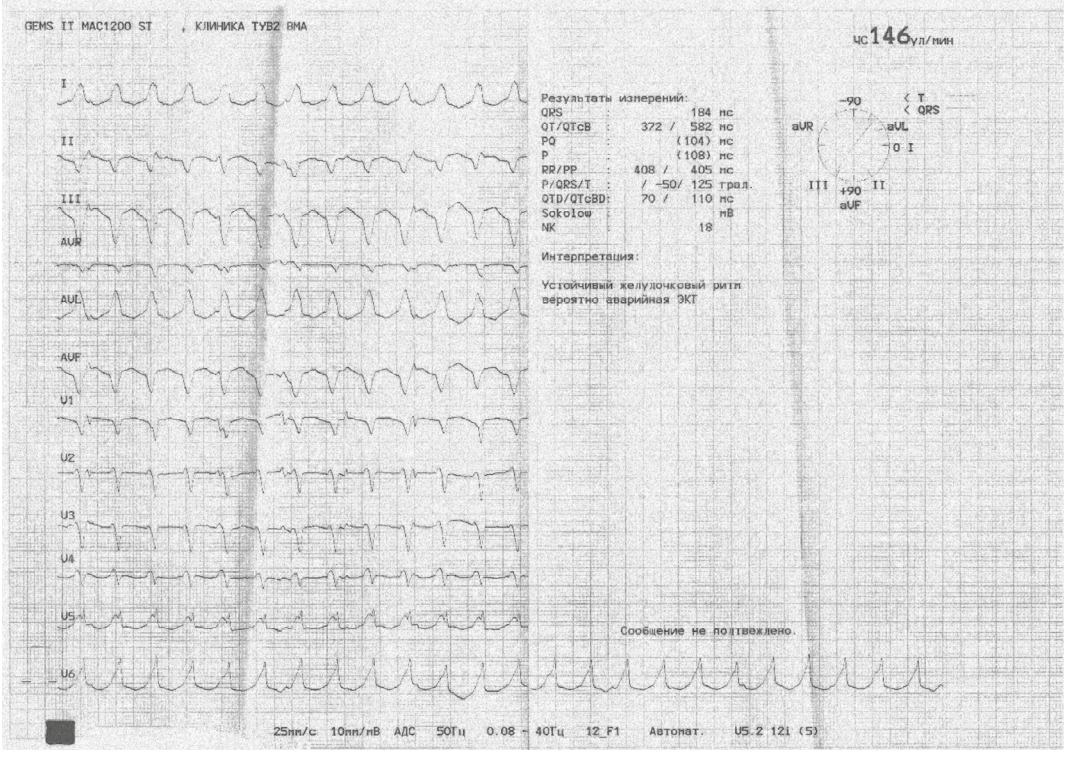


Fig. 4. Electrocardiogram of a patient suffering from right ventricular arrhythmogenic cardiomyopathy, at the time of tipical ventricular tachycardia (explanation in text)

Рис. 4. Электрокардиограмма пациента, страдающего правожелудочковой аритмогенной кардиомиопатией, во время типичной желудочковой тахикардии (объяснение в тексте)

Table 6. Recommendations for the diagnosis and management of patients suffering from arrhythmogenic cardiomyopathy
Таблица 6. Рекомендации по диагностике и ведению пациентов, страдающих аритмогенной кардиомиопатией

Recommendation	Indication class	Evidence level
Cardiac MRI is recommended for patients with suspected ACM	I	B
Genetic counseling and testing are recommended for patients with suspected or established ACM diagnosis	I	B
Patients diagnosed with ACM are advised to avoid high-intensity physical exercise	I	B
Avoidance of high-intensity physical exercise may be recommended for carriers of ACM-associated pathogenic mutations and those without the phenotype	IIb	C
Beta-blocker therapy may be recommended for all patients with an established diagnosis of ACM	IIb	C

Note: ACM — arrhythmogenic cardiomyopathy; MRI — magnetic resonance imaging.

Примечание: АКМП — аритмогенная кардиомиопатия; МРТ — магнитно-резонансная томография.

Table 7. Recommendations for risk stratification and primary prevention of sudden death in arrhythmogenic cardiomyopathy
Таблица 7. Рекомендации по стратификации риска и первичной профилактике внезапной смерт при аритмогенной кардиомиопатии

Recommendation	Indication class	Evidence level
ICD implantation is recommended for patients with a definite diagnosis of ACM and arrhythmogenic syncope	IIa	B
ICD implantation is recommended for patients with an established diagnosis of ACM and a significant decrease in RV systolic function or LV dysfunction	IIa	C
ICD implantation should be recommended in symptomatic patientsa with an established diagnosis of ACM, moderate RV or LV dysfunction or nonsustained ventricular tachycardia, or electrophysiologically induced sustained monomorphic ventricular tachycardia	IIa	C
In patients with ACM and symptoms suggestive of ventricular arrhythmia, electrophysiological testing may be recommended for risk stratification	IIb	C

Note: ACM — arrhythmogenic cardiomyopathy; ICD — implantable cardioverter defibrillator; LV — left ventricle; RV — right ventricle. [a] Presyncope or palpitations indicating ventricular arrhythmias.

Примечание: АКМП — аритмогенная кардиомиопатия; ИКД — имплантируемый кардиовертер-дефибриллятор; ЛЖ — левый желудочек; ПЖ — правый желудочек. [a] Предобморочные состояния или учащенное сердцебиение, указывающее на желудочковые аритмии.

Table 8. Recommendations for secondary prevention of sudden death and treatment of ventricular arrhythmias in arrhythmogenic cardiomyopathy
Таблица 8. Рекомендации по вторичной профилактике внезапной смерти и лечению желудочковых аритмий

Recommendation	Indication class	Evidence level
ICD implantation is recommended in patients with ACM and ventricular tachycardia or ventricular fibrillation accompanied by hemodynamic instability	I	C
In patients with ACM and nonsustained or sustained ventricular tachycardia, beta-blocker therapy is recommended	I	C
In patients with ACM and recurrent symptomatic sustained monomorphic ventricular tachycardia or ICD shocks for sustained monomorphic ventricular tachycardia despite beta-blocker therapy, catheter ablation should be recommended in specialized centers	IIa	C
Patients with ACM and indications for an ICD should be recommended to install a device with the ability to program anti-tachycardia pacing to relieve sustained monomorphic ventricular tachycardia	IIa	B
ICD implantation is recommended for patients with ACM with hemodynamically tolerated sustained monomorphic ventricular tachycardia	IIa	C
Patients with ACM and recurrent symptomatic ventricular tachycardia despite beta-blocker therapy should be treated with other antiarrhythmic agents	IIa	C

Note: ACM — arrhythmogenic cardiomyopathy; ICD — implantable cardioverter defibrillator.

Примечание: АКМП — аритмогенная кардиомиопатия; ИКД — имплантируемый кардиовертер-дефибриллятор.

Table 9. Recommendations for the management of relatives of a patient with arrhythmogenic cardiomyopathy
Таблица 9. Рекомендация по ведению родственников больного аритмогенной кардиомиопатией

Рекомендация	Класс показаний	Уровень доказательности
First-degree relatives of patients with ACM an electrocardiogram and echocardiogram are recommended	I	C

Note: ACM — arrhythmogenic cardiomyopathy.
Примечание: АКМП — аритмогенная кардиомиопатия.

RV dysfunction (EF of 40%–35%) and/or moderate LV dysfunction (EF of 45%–35%) [2].

The recommendations for the secondary prevention of sudden cardiac death and treatment of ventricular arrhythmias are presented in Table 8 [2].

Beta-blockers are recommended as first-line therapy in both symptomatic and asymptomatic cases, although this is not supported by clinical trial data [2]. Sotalol is notably effective in preventing the reproducibility of VT during electrophysiological tests [43]; however, it does not suppress clinically significant arrhythmias in real life [43, 44]. Treatment with amiodarone or class 1 drugs is associated with a trend toward lower recurrent VT rates compared with sotalol [45]. The addition of flecainide to beta-blockers or sotalol was useful in a small group of patients [46]. Note that first-class drugs are contraindicated in patients with reduced EF. Catheter ablation may be an alternative to drug therapy. When choosing a therapeutic strategy, potential risks, drug side effects, and patient preferences must be considered [47].

The recommendations for managing relatives of patients with ACM are presented in Table 9 [2].

Hypertrophic cardiomyopathy (HCM)

HCM is a disease characterized by an increase in LV wall thickness in the absence of pathological conditions associated with myocardial load, such as arterial hypertension or valvular diseases [1, 48].

Mutations in genes encoding the synthesis of sarcomeric proteins (myosin binding protein C [MYBPC3], myosin heavy chains [MYH7], cardiac troponin T [TNNT2], cardiac troponin I [TNNI3], and α-tropomyosin [TPM1], essential and regulatory light chains myosin [MYL3 and MYL2], and actin [ACTS]) are detected in 30%–60% of patients, most often in those with HCM diagnosed at a young age or with a family history of HCM [49, 50]. The recommendations emphasize the need for genetic testing of probands and screening of first-degree relatives.

In adults, the estimated prevalence of HCM is 1 per 500 populations [51]. Among children, the rate is much lower.

According to previous studies, annual mortality in HCM ranges from 0.5% to 2% [2, 48, 52]. Most HCM-associated deaths in patients aged up to 60 years occur suddenly, whereas older patients more often die from stroke, heart failure, obstruction, or supraventricular arrhythmias. The annual incidence of SCD or related ICD activation is approximately 0.8%; however, it largely depends on the age and risk profile of a patient [53–56]. SCD can also be triggered by exercise and participation in competitive sports [57].

Planning a management strategy for a patient with HCM begins with stratifying the risk of sudden cardiac death. A 5-year risk stratification scale for SCD has been developed based on seven factors, namely, age, LV wall thickness, left atrial (LA) dimension, LV outflow tract (LVOT) obstruction, nonsustained VT, unexplained syncope, and family history of SCD (HCM Risk-SCD: https://doc2do.com/hcm/webHCM.html) [2]. The calculator is not intended for evaluating professional athletes or persons with metabolic and infiltrative diseases, after myectomy or ethanol septal ablation. To stratify the risk of SCD in children (1–16 years), a special pediatric HCM risk-kids model was recently developed, including unexplained syncope, maximum LV wall thickness, LA diameter, LVOT gradient, and nonsustained VT (https://hcmriskkids.org) [2, 58].

The 2022 guidelines emphasize additional factors that are not reflected in the SCD risk model that should be considered in patients at intermediate or low estimated risk. Important additional factors include LV systolic dysfunction, aneurysm in the LV apex, extensive areas of late signal enhancement on contrast-enhanced cardiac MRI corresponding to fibrosis, and presence of single or multiple sarcomeric mutations [50, 59–64]. The identification of large areas of late MRI signal enhancement (≥15% of the LV mass) has been proposed as a good predictor of SCD. However, fibrosis thresholds are sometimes difficult to use because the quantification of late signal enhancement depends on the method by which the MR image was acquired and the type and amount of contrast used [2].

Because new risk factors may emerge in a patient's life, periodic risk reassessment is an essential part of long-term patient follow-up.

The advisability of the electrophysiological test to induce VA in HCM, according to the recommendations, is controversial because according to the literature, rhythm disturbances obtained with the electrophysiological test are considered nonspecific, although there are other points of view [65, 66].

The recommendations for risk stratification, prevention of sudden cardiac death, and treatment of ventricular arrhythmias in hypertrophic cardiomyopathy are presented in Table 10 [2].

Table 10. Recommendations for risk stratification, prevention of sudden cardiac death, and treatment of ventricular arrhythmias in hypertrophic cardiomyopathy

Таблица 10. Рекомендации по стратификации риска, профилактике внезапной сердечной смерти и лечению желудочковых аритмий при гипертрофической кардиомиопатии

Recommendation	Indication class	Evidence level
Diagnostic evaluation and general recommendations		
MRI with late gadolinium enhancement is recommended for diagnostic evaluation in a patient with HCM	I	B
Genetic counseling and testing are recommended for patients with HCM.	I	B
High-intensity exercise may be recommended in asymptomatic adult patients with HCM without risk markers for SCD	IIb	C
Risk stratification and primary prevention of SCD		
It is recommended to assess the 5-year risk of SCD at initial diagnosis and thereafter at intervals of 1–3 years or in case of a change in the patient's clinical status	I	C
ICD implantation should be recommended in patients aged 16 years or more with an estimated 5-year risk of SCD ⩾ 6%	IIa	B
ICD implantation should be recommended for HCM in patients aged 16 years or more with an intermediate 5-year risk of SCD (4%–6%) if they have the following: a) extensive late gadolinium enhancement on cardiac MRI (usually ⩾ 15% of the LV mass) or b) LVEF < 50% or c) abnormal blood pressure response during an exercise test or d) aneurysms of the LV apex or e) sarcomeric pathogenic mutation	IIa	B
ICD implantation may be recommended for HCM in patients aged 16 years or more with an estimated 5-year risk of SCD of 4%–6% without additional risk factors	IIb	B
ICD implantation may be recommended for HCM in patients aged 16 years or more with a low estimated 5-year risk of sudden cardiac death (< 4%) and a) significant late gadolinium enhancement on MRI (⩾ 15% of the LV mass); or b) LVEF < 50%; or c) LV apical aneurysm	IIb	B
In children younger than 16 years with HCM and an estimated 5-year risk of sudden death ⩾ 6% (based on the HCM rish-kids assessment), ICD implantation should be recommended	IIa	B
Secondary prevention of SCD and treatment of VA		
ICD implantation is recommended for patients with HCM with hemodynamically intolerable VT or VF	I	B
In patients with HCM and hemodynamically tolerated sustained VT, the implantation of an ICD should be recommended	IIa	C
In patients with HCM and recurrent, symptomatic VA, or recurrent ICD activations, treatment with antiarrhythmic drugs should be recommended	IIa	C
Catheter ablation in specialized centers may be recommended for some HCM patients with recurrent, symptomatic, sustained monomorphic VT or frequent ICD activation caused by sustained monomorphic VT when antiarrhythmic drugs are ineffective, intolerant, or contraindicated.	IIb	C
Management of relatives of a patient with HCM		
First-degree relatives of patients with HCM are recommended to undergo ECG and echocardiographic examination	I	C

Note: SCD — sudden cardiac death; HCM — hypertrophic cardiomyopathy; VA — ventricular arrhythmias; VT — ventricular tachycardia; ICD — implantable cardioverter defirillator; LV — left ventricle; MRI — magnetic resonance imaging; EF — ejection fraction; VF — ventricular fibrillation.

Примечание: ВСС — внезапная сердечная смерть; ГКМП — гипертрофическая кардиомиопатия; ЖА — желудочковые аритмии; ЖТ — желудочковая тахикардия; ИКД — имплантируемый кардиовертер-дефириллятор; ЛЖ — левый желудочек; МРТ — магнитно-резонансная томография; ФВ — фракция выброса; ФЖ — фибрилляция желудочков.

Patients who experience cardiac arrest due to VT/VF or hemodynamically intolerable VT are at high risk of life-threatening VA and require an ICD for secondary prevention of SCD [2, 48, 67–69]. Following ICD implantation for primary or secondary prevention of SCD, the most common documented subtype of VA is sustained monomorphic VT, in which ATP is successful in 69%–76.5% of all episodes. In this regard, during implantation, preference should be given to ICDs with ATP functionality [70–72]. No randomized clinical or cohort studies have confirmed the important role of medications in preventing SCD in HCM [2, 48, 73]. Amiodarone can reduce the number of VA; however, data on its effectiveness in preventing SCD are inconsistent [73, 74]. Disopyramide and beta-blockers are effective in controlling symptoms and LVOT obstruction; however, no evidence shows that they reduce the risk of SCD [2, 48]. Similarly, surgical myectomy or ethanol ablation is not recommended to reduce the SCD risk in patients with LVOT obstruction [2, 48]. Despite the lack of clear data on the efficiency of antiarrhythmic drugs, beta-blockers, amiodarone, sotalol, and sodium channel blockers are prescribed to patients with HCM and symptomatic VAs [2]. Catheter ablation may also be used in carefully selected patients with HCM and sustained monomorphic VT for whom antiarrhythmic drugs are ineffective, contraindicated, or intolerable. The recommendations emphasize that the results after ablation for HCM are worse than those for other diseases of nonischemic etiology [75–77].

Left ventricular non-compaction (LVNC)

Since 1995, along with HCM, DCM, RCM, and ACM, a group of "unclassified" cardiomyopathies has been identified, including LVNC or noncompact cardiomyopathy (NCM) and Takotsubo syndrome. In the 2023 European Society of Cardiology guidelines on cardiomyopathies, the concept of "unclassified" cardiomyopathies was abolished and replaced by "syndromes associated with cardiomyopathic phenotypes" [15]. Taking into account the change in the approach to the classification of cardiomyopathies, the 2023 recommendations propose using the term "left ventricle hypertrabecularity" instead of LVNC.

In this article, we use the term LVNC because this is the term used in the 2022 European guidelines for the treatment of ventricular arrhythmias and the prevention of SCD. LVNC includes a heterogeneous group of phenotypically different diseases characterized by specific changes in the LV myocardium and sometimes RV myocardium [2, 78–80]. A structural pathology common to all phenotypes is abnormal trabeculae in the LV/RV or both ventricles, most often in the apical region [78–80]. Figure 5 presents an echocardiogram of one of our patients.

LVNC may include LV dilatation, LV hypertrophy, systolic dysfunction, diastolic dysfunction, or both, and it may be associated with various congenital heart defects [78–80].

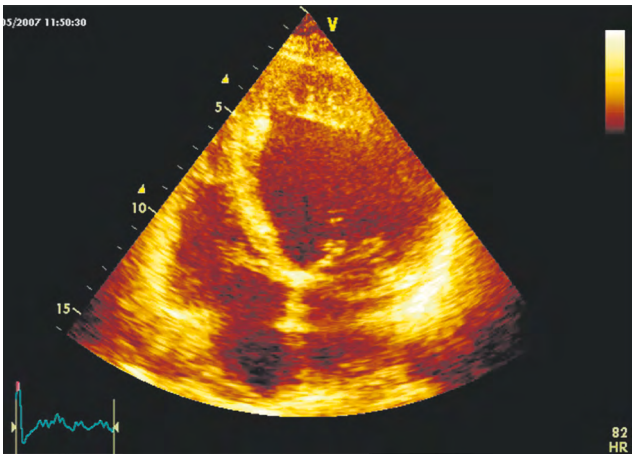


Fig. 5. Echocardiogram of a patient with left ventricular hypertrabeculation. Apical 4-chamber view. Noteworthy is the dilatation of the left ventricle and pronounced trabecularity in the area at the apex

Рис. 5. Эхокардиограмма пациента, имеющего гипертрабекулярность миокарда левого желудочка. Верхушечная 4-камерная позиция. Обращают на себя внимание дилатация левого желудочка и выраженная трабекулярность в области верхушки

Clinically, the disease manifests as CHF, life-threatening VAs, complete AV block, and bundle branch blocks. Up to nine variants of the disease, hemodynamically and clinically occurring differently [79, 80]:

1) Isolated or benign form: LVNC with structural changes, absent hemodynamic disturbances, and clinical signs (registered in athletes and pregnant women);

2) Arrhythmogenic form: the main clinical manifestation is cardiac arrhythmia, primarily VA;

3) Dilated form: in addition to characteristic morphological changes, there is dilation and decreased contractility of the LV;

4) Hypertrophic form, with no pronounced dilatation, but with myocardial hypertrophy, primarily thickening of the myocardium, which is not involved in the noncompaction process;

5) "Mixed" form of non-compaction;

6) Restrictive form, in which severe diastolic dysfunction predominates;

7) Biventricular form of the non-compaction;

8) Excessive trabecularity of the RV with a normal structure of the LV;

9) Combination of non-compaction with congenital heart defects.

The association of the disease with genetic abnormalities is detected in 30%–50% of patients. Several genes encoding sarcomeric or cytoskeletal proteins have been identified; however, the identified genetic abnormalities occur not only in NCM but also in other cardiomyopathies, including Barth syndrome [79, 80].

Diagnostics of non-compaction are difficult; various proposed diagnostic criteria have not yet been validated, and

Table 11. Recommendations for cardioverter defibrillator implantation in left ventricular non-compaction
Таблица 11. Рекомендации по имплантации кардиовертера-дефибриллятора при некомпактном миокарде левого желудочка

Recommendation	Indication class	Evidence level
In patients with noncompact cardiomyopathy diagnosed according to MRI or echocardiographic findings, ICD implantation should be recommended for primary prevention of SCD for the same indications as for DCM/HNDCM.	IIa	C

Note: SCD — sudden cardiac death; DCM — dilated cardiomyopathy; HNDCM — hypokinetic nondilated cardiomyopathy; ICD — implantable cardioverter defibrillator, MRI — magnetic resonance imaging.

Примечание: ВСС — внезапная сердечная смерть; ДКМП — дилатационная кардиомиопатия; ГНДКМП — гипокинетическая недилатационная кардиомиопатия; ИКД — имплантируемый кардиовертер-дефибриллятор: МРТ — магнитно-резонансная томография.

Table 12. Recommendations for implantation of a cardioverter-defibrillator in patients with cardiac amyloidosis
Таблица 12. Рекомендации по имплантации кардиовертера-дефибриллятора пациентам, страдающим амилоидозом сердца

Recommendation	Indication class	Evidence level
ICD should be recommended in patients with light-chain amyloidosis or transthyretin-associated amyloid CMP and hemodynamically intolerable VT	IIa	C

Note: VT — ventricular tachycardia; ICD — implantable cardioverter defibrillator; CMP — cardiomyopathy.

Примечание: ЖТ — желудочковая тахикардия; ИКД — имплантируемый кардиовертер-дефибриллятор; КМП — кардиомиопатия.

none of them are given as diagnostic criteria in the recommendations. Cardiovascular mortality in patients with NCM is similar to that in patients with DCM [81]. The detection of focal fibrosis on contrast-enhanced MRI is associated with serious cardiovascular events, including arrhythmic events [82]. However, the risk stratification criteria for SCD in NCM have not yet been developed. Thus, in the future, combining MRI criteria with genetic testing data may overcome the current uncertainty regarding risk stratification for adverse events in NCM [2, 83]. In the meantime, when deciding on ICD implantation for diagnosed NCM, the criteria recommended for DCM/HNDCM should be used. The recommendations for ICD implantation for LVNC are presented in Table 11 [2].

Restrictive cardiomyopathy (RCM)

The RCM phenotype is rare and can result from various causes, including genetically determined and acquired interstitial fibrosis, infiltrative disorders (e.g., amyloidosis), and storage diseases (e.g., Anderson–Fabry disease). Their identification is crucial for the choice of therapy because of certain diseases in which in the clinical course restrictive hemodynamics comes to the fore, and there is a specific disease-modifying therapy. Heart failure is a major symptom of any type of RCM. Depending on the phenotype, atrial or ventricular arrhythmias may predominate, including fatal ones. For example, in Fabry disease, the most reported cardiovascular deaths were classified as SCD [84]. Because RCM is the rarest among all CMPs, large randomized studies of this pathology are not yet available. The retrospective, observational nature of most minor, single-center studies and the low absolute number of deaths due to cardiovascular disease and SCD in these studies do not currently allow ICDs to be recommended for the primary prevention of SCD in RCM. The guidelines provide advice only ICD for cardiac amyloidosis (Table 12) [2]. Currently, an ICD should be recommended for patients with amyloid CMP and hemodynamically intolerable VT after careful consideration of the competing risks of nonarrhythmic and noncardiac death.

Recommendations devoted to the urgent issues of determining CMP, diagnostics, risk stratification of SCD, and treatment of VA in CMPs are of great practical interest because fatal ventricular arrhythmias are a common complication of all CMPs.

ADDITIONAL INFORMATION

Competing interests. The authors declare that they have no competing interests.

Funding source. This study was not supported by any external sources of funding.

ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Источник финансирования. Авторы заявляют об отсутствии внешнего финансирования при проведении исследования.

REFERENSES

1. Elliott P, Andersson B, Arbustini E, et al. Classification of the cardiomyopathies: a position statement from the European Society Of Cardiology Working Group on Myocardial and Pericardial Diseases. *European Heart Journal.* 2008;29:270–276. DOI: https://doi.org/10.1093/eurheartj/ehm342

2. Zeppenfeld K, Tfelt-Hansen J, de Riva M, et al. 2022 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death. *European Heart Journal.* 2022;00:1–130. DOI: https://doi.org/10.1093/eurheartj/ehac262

3. Køber L, Thune JJ, Nielsen JC, et al. Defibrillator implantation in patients with nonischemic systolic heart failure. *The New England Journal of Medicine.* 2016;375:1221–1230. DOI: https://doi.org/10.1056/NEJMoa1608029

4. Weintraub RG, Semsarian C, Macdonald P. Dilated cardiomyopathy. *Lancet.* 2017;390:400–414. DOI: https://doi.org/10.1016/S0140-6736(16)31713-5

5. Beggs SAS., Jhund PS, Jackson CE, et al. Non-ischaemic cardiomyopathy, sudden death and implantable defibrillators: a review and meta-analysis. *Heart.* 2018;104:144–150. DOI: https://doi.org/10.1136/heartjnl-2016-310850

6. Codd MB, Sugrue DD, Gersh BJ, Melton LJ. Epidemiology of idiopathic dilated and hypertrophic cardiomyopathy. A population-based study in Olmsted County, Minnesota, 1975–1984. *Circulation.* 1989;80:564–572. DOI: https://doi.org/10.1161/01.cir.80.3.564

7. Manolio TA, Baughman KL, Rodeheffer R, et al. Prevalence and etiology of idiopathic dilated cardiomyopathy (summary of a National Heart, Lung, and Blood Institute workshop. *Americal Journal of Cardiology.* 1992;69:1458–1466. DOI: https://doi.org/10.1016/0002-9149(92)90901-a

8. Pinto YM, Elliott PM, Arbustini E, et al. Proposal for a revised definition of dilated cardiomyopathy, hypokinetic non-dilated cardiomyopathy, and its implications for clinical practice: a position statement of the ESC working group on myocardial and pericardial diseases. *European Heart Journal.* 2016;37(23):1850–1858. DOI: https://doi.org/10.1093/eurheartj/ehv727

9. Zhang X-L, Xie J, Lan R-F, et al. Genetic Basis and Genotype–Phenotype Correlations in Han Chinese Patients with Idiopathic Dilated Cardiomyopathy. *Scientific Reports.* 2020;10:2226. DOI: https://doi.org/10.1038/s41598-020-58984-7.

10. Ader F, De Groote P, Réant P, et al. FLNC pathogenic variants in patients with cardiomyopathies: prevalence and genotype-phenotype correlations. *Clinical Genetics.* 2019;96:317–329. DOI: https://doi.org/10.1111/cge.13594

11. Kayvanpour E, Sedaghat-Hamedani F, Amr A, et al. Genotype-phenotype associations in dilated cardiomyopathy: meta-analysis on more than 8000 individuals. *Clinical Research in Cardiology.* 2017;106:127–139. DOI: https://doi.org/10.1007/s00392-016-1033-6

12. Ortiz-Genga MF, Cuenca S, Dal Ferro M, et al. Truncating FLNC mutations are associated with high-risk dilated and arrhythmogenic cardiomyopathies. *Journal of the American College of Cardiology.* 2016;68:2440–2451. DOI: https://doi.org/10.1016/j.jacc.2016.09.927

13. van den Hoogenhof MMG, Beqqali A, Amin AS, et al. RBM20 mutations induce an arrhythmogenic dilated cardiomyopathy related to disturbed calcium handling. *Circulation.* 2018;138:1330–1342. DOI: https://doi.org/10.1161/CIRCULATIONAHA.117.031947

14. Gigli M, Merlo M, Graw SL, et al. Genetic risk of arrhythmic phenotypes in patients with dilated cardiomyopathy. *Journal of the American College of Cardiology.* 2019;74:1480–1490. DOI: https://doi.org/10.1016/j.jacc.2019.06.072

15. Arbelo E, Protonotarios A, Gimeno JR, et al. 2023 ESC Guidelines for the management of cardiomyopathies. *European Heart Journal.* 2023;44(37):1–124. DOI: https://doi.org/10.1093/eurheartj/ehad194

16. Iles LM, Ellims AH, Llewellyn H, et al. Histological validation of cardiac magnetic resonance analysis of regional and diffuse interstitial myocardial fibrosis. *European Heart Journal–Cardiovascular Imaging.* 2015;16:14–22. DOI: https://doi.org/10.1093/ehjci/jeu182

17. Olivas-Chacon CI, Mullins C, Stewart K, et al. Magnetic Resonance Imaging of Non-ischemic Cardiomyopathies: A Pictorial Essay. *Pictorial Essay.* 2015;5:37. DOI: https://doi.org/10.4103/2156-7514.159564

18. Di Marco A, Anguera I, Schmitt M, et al. Late gadolinium enhancement and the risk for ventricular arrhythmias or sudden death in dilated cardiomyopathy: systematic review and meta-analysis. *JACC: Heart Fail.* 2017;5:28–38. DOI: https://doi.org/10.1016/j.jchf.2016.09.017

19. Klem I, Klein M, Khan M, et al. Relationship of LVEF and myocardial scar to long-term mortality risk and mode of death in patients with nonischemic cardiomyopathy. *Circulation.* 2021:143:1343–1358. DOI: https://doi.org/10.1161/CIRCULATIONAHA.120.048477

20. Goidescu CM. Dilated cardiomyopathy produced by lamin A/C gene mutations. *Cluju Med.* 2013;86(4):309–312.

21. Connolly SJ, Dorian P, Roberts RS, et al. Comparison of beta-blockers, amiodarone plus beta-blockers, or sotalol for prevention of shocks from implantable cardioverter defibrillators: the OPTIC Study: a randomized trial. *JAMA.* 2006;295:165–171. DOI: https://doi.org/10.1001/jama.295.2.165

22. Dinov B, Fiedler L, Schönbauer R, et al. Outcomes in catheter ablation of ventricular tachycardia in dilated nonischemic cardiomyopathy compared with ischemic cardiomyopathy: results from the Prospective Heart Centre of Leipzig VT (HELP-VT) Study. *Circulation.* 2014;129:728–736. DOI: https://doi.org/10.1161/CIRCULATIONAHA.113.003063

23. Muser D, Santangeli P, Castro SA, et al. Long-term outcome after catheter ablation of ventricular tachycardia in patients with nonischemic dilated cardiomyopathy. *Circulation Arrhythmia and Electrophysiology.* 2016;9:004328. DOI: https://doi.org/10.1161/CIRCEP.116.004328

24. Ebert M, Richter S, Dinov B, et al. Evaluation and management of ventricular tachycardia in patients with dilated cardiomyopathy. *Heart Rhythm.* 2019;16:624–631. DOI: https://doi.org/10.1016/j.hrthm.2018.10.028

25. Kumar S, Androulakis AFA, Sellal J-M, et al. Multicenter experience with catheter ablation for ventricular tachycardia in lamin A/C cardiomyopathy. *Circulation Arrhythmia and Electrophysiology.* 2016;9:004357. DOI: https://doi.org/ 10.1161/CIRCEP.116.004357

26. Oloriz T, Silberbauer J, Maccabelli G, et al. Catheter ablation of ventricular arrhythmia in nonischemic cardiomyopathy: anteroseptal versus inferolateral scar sub-types. *Circulation Arrhythmia and Electrophysiology.* 2014;7:414–423. DOI: https://doi.org/10.1161/CIRCEP.114.001568

27. Corrado D, Link MS, Calkins H. Arrhythmogenic right ventricular cardiomyopathy. *The New England Journal of Medicine*. 2017;376:1489–1490. DOI: https://doi.org/10.1056/NEJMra1509267

28. Corrado D, Marra MP, Zorzi A, et al. Diagnosis of arrhythmogenic cardiomyopathy: The Padua criteria. *International Journal of Cardiology*. 2020;319:106–114. DOI: https://doi.org/10.1016/j.ijcard.2020.06.005.

29. Mazzanti A, Ng K, Faragli A, et al. Arrhythmogenic right ventricular cardiomyopathy: clinical course and predictors of arrhythmic risk. *Journal of the American College of Cardiology*. 2016;68:2540–2550. DOI: https://doi.org/10.1016/j.jacc.2016.09.951

30. Bhonsale A, Groeneweg JA, James CA, et al. Impact of genotype on clinical course in arrhythmogenic right ventricular dysplasia/cardiomyopathy-associated mutation carriers. *European Heart Journal*. 2015;36:847–855. DOI: https://doi.org/10.1093/eurheartj/ehu509

31. Rigato I, Bauce B, Rampazzo A, et al. Compound and digenic heterozygosity predicts life time arrhythmic outcome and sudden cardiac death in desmosomal gene-related arrhythmogenic right ventricular cardiomyopathy. *Circulation Cardiovascular Genetics*. 2013;6:533–542. DOI: https://doi.org/10.1161/CIRCGENETICS.113.000288

32. Novikova TN, Novikov VI, Sayganov SA, Shcherbakova VA. 2022 Esc guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: what is new? *Cardiac Arrhythmias*. 2022;2(3):7–30. DOI.org/10.17816/cardar110961

33. Hulot J-S, Jouven X, Empana J-P, et al. Natural history and risk stratification of arrhythmogenic right ventricular dysplasia/cardiomyopathy. *Circulation*. 2004;110:1879–1884. DOI: https://doi.org/10.1161/01.CIR.0000143375.93288.82

34. Wang W, Cadrin-Tourigny J, Bhonsale A, et al. Arrhythmic outcome of arrhythmogenic right ventricular cardiomyopathy patients without implantable defibrillators. *Journal of Cardiovascular Electrophysiology*. 2018;29:1396–1402. DOI: https://doi.org/10.1111/jce.13668

35. Pinamonti ., Dragos AM, Pyxaras SA, et al. Prognostic predictors in arrhythmogenic right ventricular cardiomyopathy: results froma 10-year registry. *European Heart Journal*. 2011;32:1105–1113. DOI: https://doi.org/10.1093/eurheartj/ehr040

36. Brun F, Groeneweg JA, Gear K, et al. Risk stratification in arrhythmic right ventricular cardiomyopathy without implantable cardioverter-defibrillators. *JACC Clinical Electrophysiology*. 2016;2:558–564. DOI: https://doi.org/10.1016/j.jacep.2016.03.015

37. Bhonsale A, James CA, Tichnell C, et al. Incidence and predictors of implantable cardioverter-defibrillator therapy in patients with arrhythmogenic right ventricular dysplasia/cardiomyopathy undergoing implantable cardioverter-defibrillator implantation for primary prevention. *Journal of the American College of Cardiology*. 2011;58:1485–1496. DOI: https://doi.org/10.1016/j.jacc.2011.06.043

38. Corrado D, Calkins H, Link MS, et al. Prophylactic implantable defibrillator in patients with arrhythmogenic right ventricular cardiomyopathy/dysplasia and no prior ventricular fibrillation or sustained ventricular tachycardia. *Circulation*. 2010;122:1144–1152. DOI: https://doi.org/10.1161/CIRCULATIONAHA.109.913871

39. Platonov PG, Haugaa KH, Bundgaard H, et al. Primary prevention of sudden cardiac death with implantable cardioverter-defibrillator therapy in patients with arrhythmogenic right ventricular cardiomyopathy. *American Journal of Cardiology*. 2019;123:1156–1162. DOI: https://doi.org/10.1016/j.amjcard.2018.12.049

40. Link MS, Laidlaw D, Polonsky B, et al. Ventricular arrhythmias in the North American multidisciplinary study of ARVC: predictors, characteristics, and treatment. *Journal of the American College of Cardiology*. 2014;64:119–125. DOI: https://doi.org/10.1016/j.jacc.2014.04.035

41. Cadrin-Tourigny J, Bosman LP, Nozza A, et al. A new prediction model for ventricular arrhythmias in arrhythmogenic right ventricular cardiomyopathy. *European Heart Journal*. 2019;40:1850–1858. DOI: https://doi.org/10.1093/eurheartj/ehz103

42. Cadrin-Tourigny J, Bosman LP, Wang W, et al. Sudden cardiac death prediction in arrhythmogenic right ventricular cardiomyopathy: a multinational collaboration. *Circulation Arrhythmia and Electrophysiology*. 2021;14:008509. DOI: https://doi.org/10.1161/CIRCEP.120.008509

43. Wichter T, Borggrefe M, Haverkamp W, et al. Efficacy of antiarrhythmic drugs in patients with arrhythmogenic right ventricular disease. Results in patients with inducible and noninducible ventricular tachycardia. *Circulation*. 1992;86:29–37. DOI: https://doi.org/10.1161/01.cir.86.1.29

44. Marcus GM, Glidden DV, Polonsky B, et al. Efficacy of antiarrhythmic drugs in arrhythmogenic right ventricular cardiomyopathy: a report from the North American ARVC Registry. *Journal of the American College of Cardiology*. 2009;54:609–615. DOI: https://doi.org/10.1016/j.jacc.2009.04.052

45. Mahida S, Venlet J, Saguner AM, et al. Ablation compared with drug therapy for recurrent ventricular tachycardia in arrhythmogenic right ventricular cardiomyopathy: results from a multicenter study. *Heart Rhythm*. 2019;16:536–543. DOI: https://doi.org/10.1016/j.hrthm.2018.10.016

46. Ermakov S, Gerstenfeld EP, Svetlichnaya Y, Scheinman MM. Use of flecainide in combination antiarrhythmic therapy in patients with arrhythmogenic right ventricular cardiomyopathy. *Heart Rhythm*. 2017;14:564–569. DOI: https://doi.org/10.1016/j.hrthm.2016.12.010

47. Santangeli P, Zado ES, Supple GE, et al. Long-term outcome with catheter ablation of ventricular tachycardia in patients with arrhythmogenic right ventricular cardiomyopathy. *Circulation Arrhythmia and Electrophysiology*. 2015;8:1413–1421. DOI: https://doi.org/10.1161/CIRCEP.115.003562

48. Ommen SR, Mital S, Burke MA, et al. 2020 AHA/ACC guideline for the diagnosis and treatment of patients with hypertrophic cardiomyopathy: executive summary: a report of the American College of Cardiology/ American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation*. 2020;142:533–557. DOI: https://doi.org/10.1161/CIR.0000000000000938

49. Heliö T, Elliott P, Koskenvuo JW, et al. ESC EORP cardiomyopathy registry: real-life practice of genetic counselling and testing in adult cardiomyopathy patients. *ESC Heart Failure*. 2020;7:3013–3021. DOI: https://doi.org/10.1002/ehf2.12925

50. Ho CY, Day SM, Ashley EA, et al. Genotype and life time burden of disease in hypertrophic cardiomyopathy: insights from the Sarcomeric Human Cardiomyopathy Registry (SHaRe). *Circulation*. 2018;138:1387–1398. DOI: https://doi.org/10.1161/CIRCULATIONAHA.117.033200

51. Semsarian C, Ingles J, Maron MS, Maron BJ. New perspectives on the prevalence of hypertrophic cardiomyopathy. *Journal of the American College of Cardiology*. 2015;65:1249–1254. DOI: https://doi.org/10.1016/j.jacc.2015.01.019

52. Maron BJ, Rowin EJ, Casey SA, et al. Hypertrophic cardiomyopathy in adulthood as sociated with low cardiovascular

mortality with contemporary management strategies. *Journal of the American College of Cardiology*. 2015;65:1915–1928. DOI: https://doi.org/10.1016/j.jacc.2015.02.061

53. O'Mahony C, Jichi F, Pavlou M, et al. A novel clinical risk prediction model for sudden cardiac death in hypertrophic cardiomyopathy (HCMrisk-SCD). *European Heart Journal*. 2014;35:2010–2020. DOI: https://doi.org/10.1093/eurheartj/eht439

54. O'Mahony C, Jichi F, Ommen SR, et al. International External Validation Study of the 2014 European Society of Cardiology Guidelines on Sudden Cardiac Death Prevention in Hypertrophic Cardiomyopathy (EVIDENCE-HCM). *Circulation*. 2018;137:1015–1023. DOI: https://doi.org/10.1161/CIRCULATIONAHA.117.030437

55. Vriesendorp PA, Schinkel AFL, Liebregts M, et al. Validation of the 2014 European Society of Cardiology guidelines risk prediction model for the primary revention of sudden cardiac death in hypertrophic cardiomyopathy. *Circulation Arrhythmia and Electrophysiology*. 2015;8:829–835. DOI: https://doi.org/10.1161/CIRCEP.114.002553

56. Lorenzini M, Anastasiou Z, O'Mahony C, et al. Mortality among referral patients with hypertrophic cardiomyopathy vs the general European population. *JAMA Cardiology*. 2020;5:73–80. DOI: https://doi.org/10.1001/jamacardio.2019.4534

57. Gimeno JR, Tomé-Esteban M, Lofiego C, et al. Exercise-induced ventricular arrhythmias and risk of sudden cardiac death in patients with hypertrophic cardiomyopathy. *European Heart Journal*. 200;30:2599–2605. DOI: https://doi.org/10.1093/eurheartj/ehp327

58. Norrish G, Qu C, Field E, et al. External validation of the HCM Risk-Kids model for predicting sudden cardiac death in childhood hypertrophic cardiomyopathy. *European Journal of Preventive Cardiology*. 2022;29:678–686. DOI: https://doi.org/10.1093/eurjpc/zwab181

59. Chan RH, Maron BJ, Olivotto I, et al. Prognostic value of quantitative contrast-enhanced cardiovascular magnetic resonance for the evaluation of sudden death risk in patients with hypertrophic cardiomyopathy. *Circulation*. 2014;130:484–495. DOI: https://doi.org/10.1161/CIRCULATIONAHA.113.007094

60. He D, Ye M, Zhang L, Jiang B. Prognostic significance of late gadolinium enhancement on cardiac magnetic resonance in patients with hypertrophic cardiomyopathy. *Heart Lung*. 2018;47:122–126. DOI: https://doi.org/10.1016/j.hrtlng.2017.10.008

61. Rowin EJ, Maron BJ, Carrick RT, et al. Outcomes in patients with hypertrophic cardiomyopathy and left ventricular systolic dysfunction. *Journal of the American College of Cardiology*. 2020;75:3033–3043. DOI: https://doi.org/10.1016/j.jacc.2020.04.045

62. Rowin EJ, Maron BJ, Haas TS, et al. Hypertrophic cardiomyopathy with left ventricular apical aneurysm: implications for risk stratification and management. *Journal of the American College of Cardiology*. 2017;69:761–773. DOI: https://doi.org/10.1016/j.jacc.2016.11.063

63. Sadoul N, Prasad K, Elliott PM, et al. Prospective prognostic assessment of blood pressure response during exercise in patients with hypertrophic cardiomyopathy. *Circulation*. 1997;96:2987–2991. DOI: https://doi.org/10.1161/01.cir.96.9.2987

64. Elliott PM, Poloniecki J, Dickie S, et al. Sudden death in hypertrophic cardiomyopathy: identification of high risk patients. *Journal of the American College of Cardiology*. 2000;36:2212–2218. DOI: https://doi.org/10.1016/s0735-1097(00)01003-2

65. Behr ER, Elliott P, McKenna WJ. Role of invasive EP testing in the evaluation and management of hypertrophic cardiomyopathy. *Cardiac Electrophysiology Review*. 2002;6:482–486. DOI: https://doi.org/10.1023/a:1021161114347

66. Gatzoulis KA, Georgopoulos S, Antoniou C-K, et al. Programmed ventricular stimulation predicts arrhythmic events and survival in hypertrophic cardiomyopathy. *International Journal of Cardiology*. 2018;254:175–181. DOI: https://doi.org/10.1016/j.ijcard.2017.10.033

67. Elliott PM, Sharma S, Varnava A, et al. Survival after cardiac arrest or sustained ventricular tachycardia in patients with hypertrophic cardiomyopathy. *Journal of the American College of Cardiology*. 1999;33:1596–1601. DOI: https://doi.org/10.1016/s0735-1097(99)00056-x

68. Cecchi F, Maron BJ, Epstein SE. Long-term outcome of patients with hypertrophic cardiomyopathy successfully resuscitated after cardiac arrest. *Journal of the American College of Cardiology*. 1989; 13:1283–1288. DOI: https://doi.org/10.1016/0735-1097(89)90302-1

69. Maron BJ, Spirito P, Shen W-K, et al. Implantable cardioverter-defibrillators and prevention of sudden cardiac death in hypertrophic cardiomyopathy. *JAMA*. 2007;298:405–412. DOI: https://doi.org/10.1001/jama.298.4.405

70. Link MS, Bockstall K, Weinstock J, et al. Ventricular tachyarrhythmias in patients with hypertrophic cardiomyopathy and defibrillators: triggers, treatment, and implications. *Journal of Cardiovascular Electrophysiology*. 2017;28:531–537. DOI: https://doi.org/10.1111/jce.13194

71. Dallaglio PD, DiMarco A, MorenoWeidmann Z, et al. Antitachycardia pacing for shock prevention in patients with hypertrophic cardiomyopathy and ventricular tachycardia. *Heart Rhythm*. 2020;17:1084–1091. DOI: https://doi.org/10.1016/j.hrthm.2020.02.024

72. Adduci C, Semprini L, Palano F, et al. Safety and efficacy of antitachycardia pacing in patients with hypertrophic cardiomyopathy implanted with an ICD. *Pacing and Clinical Electrophysiology*. 2019;42:610–616. DOI: https://doi.org/10.1111/pace.13665

73. Melacini P, Maron BJ, Bobbo F, et al. Evidence that pharmacological strategies lack efficacy for the prevention of sudden death in hypertrophic cardiomyopathy. *Heart*. 2007;93:708–710. DOI: https://doi.org/10.1136/hrt.2006.099416

74. McKenna WJ, Oakley CM, Krikler DM, Goodwin JF. Improved survival with amiodarone in patients with hypertrophic cardiomyopathy and ventricular tachycardia. *British Heart Journal*. 1985;53:412–416. DOI: https://doi.org/10.1136/hrt.53.4.412

75. Vaseghi M, Hu TY, Tung R, et al. Outcomes of catheter ablation of ventricular tachycardia based on etiology in nonischemic heart disease: an international ventricular tachycardia ablation center collaborative study. *JACC Clinical Electrophysiology*. 2018;4: 1141–1150. DOI: https://doi.org/10.1016/j.jacep.2018.05.007

76. Igarashi M, Nogami A, Kurosaki K, et al. Radiofrequency catheter ablation of ventricular tachycardia in patients with hypertrophic cardiomyopathy and apical aneurysm. *JACC Clinical Electrophysiology*. 2018;4:339–350. DOI: https://doi.org/10.1016/j.jacep.2017.12.020

77. Dukkipati SR, d'Avila A, Soejima K, et al. Long-term outcomes of combined epicardial and endocardial ablation of monomorphic ventricular tachycardia related to hypertrophic cardiomyopathy. *Circulation Arrhythmia and Electrophysiology*. 2011;4:185–194. DOI: https://doi.org/10.1161/CIRCEP.110.957290

78. Novikov VI, Novikova TN. *Cardiomyopathy*. Moscow: MEDpress-inform 2021;112 (In Russ.)

79. Towbin JA, Lorts A, Jefferies JL. Left ventricular non-compaction cardiomyopathy. *Lancet*. 2015;386(9995):813-25. DOI: https://doi.org/10.1016/S0140-6736(14)61282-4.

80. Gerecke BJ, Engberding R. Noncompaction Cardiomyopathy – History and Current Knowledge for Clinical Practice. *Journal of Clinical Medicine*. 2021;10(11):2457. DOI: https://doi.org/10.3390/jcm10112457.

81. Aung N, Doimo S, Ricci F, et al. Prognostic significance of left ventricular noncompaction: systematic review and meta-analysis of observational studies. *Circulation Cardiovascular Imaging*. 2020;13:009712. DOI: https://doi.org/10.1161/CIRCIMAGING.119.009712

82. Grigoratos C, Barison A, Ivanov A, et al. Meta-analysis of the prognostic role of late gadolinium enhancement and global systolic impairment in left ventricular noncompaction. *JACC Cardiovascular Imaging*. 2019;12:2141–2151. DOI: https://doi.org/10.1016/j.jcmg.2018.12.029

83. Richard P, Ader F, Roux M, et al. Targeted panel sequencing in adult patients with left ventricular non-compaction reveals a large genetic heterogeneity. *Clinical Genetics*. 2019;95:356–367. DOI: https://doi.org/10.1111/cge.13484

84. Baig S, Edward NC, Kotecha D, et al. Ventricular arrhythmia and sudden cardiac death in Fabry disease: a systematic review of risk factors in clinical practice. *Europace*. 2018;20:153–161. DOI: https://doi.org/10.1093/europace/eux261

СПИСОК ЛИТЕРАТУРЫ

1. Elliott P., Andersson B., Arbustini E., et al. Classification of the cardiomyopathies: a position statement from the European Society Of Cardiology Working Group on Myocardial and Pericardial Diseases // Eur Heart J. 2008. Vol. 29. P. 270–276. DOI: https://doi.org/10.1093/eurheartj/ehm342

2. Zeppenfeld K., Tfelt-Hansen J., de Riva M., et al. 2022 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death // European Heart J. 2022. Vol. 43, No. 40. P. 3997–4126. DOI: https://doi. org/10.1093/eurheartj/ehac262

3. Køber L., Thune J.J., Nielsen J.C., et al. Defibrillator implantation in patients with nonischemic systolic heart failure // N Engl J. Med. 2016. Vol. 375. P. 1221–1230. DOI: https://doi.org/10.1056/NEJMoa1608029

4. Weintraub R.G., Semsarian C., Macdonald P. Dilated cardiomyopathy // Lancet. 2017. Vol. 390. P. 400–414. DOI: https://doi.org/10.1016/S0140-6736(16)31713-5

5. Beggs S.A.S., Jhund P.S., Jackson C.E., et al. Non-ischaemic cardiomyopathy, sudden death and implantable defibrillators: a review and meta-analysis // Heart. 2018. Vol. 104. P. 144–150. DOI: https://doi.org/10.1136/heartjnl-2016-310850

6. Codd M.B., Sugrue D.D., Gersh B.J., Melton L.J. Epidemiology of idiopathic dilated and hypertrophic cardiomyopathy. A population-based study in Olmsted County, Minnesota, 1975–1984 // Circulation. 1989. Vol. 80. P. 564–572. DOI: https://doi.org/10.1161/01.cir.80.3.564

7. Manolio T.A., Baughman K.L., Rodeheffer R., et al. Prevalence and etiology of idiopathic dilated cardiomyopathy (summary of a National Heart, Lung, and Blood Institute workshop // Am J Cardiol. 1992. Vol. 69. P. 1458–1466. DOI: https://doi.org/10.1016/0002-9149(92)90901-a

8. Pinto Y.M., Elliott P.M., Arbustini E., et al. Proposal for a revised definition of dilated cardiomyopathy, hypokinetic non-dilated cardiomyopathy, and its implications for clinical practice: a position statement of the ESC working group on myocardial and pericardial diseases // Eur Heart J. 2016. Vol. 37(23). P. 1850–1858. DOI: https://doi.org/10.1093/eurheartj/ehv727.

9. Zhang X.-L., Xie J., Lan R.-F., et al. Genetic Basis and Genotype–Phenotype Correlations in Han Chinese Patients with Idiopathic Dilated Cardiomyopathy // Scientific Reports. 2020. Vol. 10. P. 2226. DOI: https://doi.org/10.1038/s41598-020-58984-7.

10. Ader F., De Groote P., Réant P., et al. FLNC pathogenic variants in patients with cardiomyopathies: prevalence and genotype-phenotype correlations // Clin Genet. 2019. Vol. 96. P. 317–329. DOI: https://doi/10.1111/cge.13594

11. Kayvanpour E., Sedaghat-Hamedani F., Amr A., et al. Genotype-phenotype associations in dilated cardiomyopathy: meta-analysis on more than 8000 individuals // Clin Res Cardiol. 2017. Vol. 106. P. 127–139. DOI: https://doi.org/10.1007/s00392-016-1033-6

12. Ortiz-Genga M.F., Cuenca S., Dal Ferro M., et al. Truncating FLNC mutations are associated with high-risk dilated and arrhythmogenic cardiomyopathies // J Am Coll Cardiol. 2016. Vol. 68. P. 2440–2451. DOI: https://doi.org/10.1016/j.jacc.2016.09.927

13. Earrhythmogenic dilated cardiomyopathy related to disturbed calcium handling // Circulation. 2018. Vol. 138. P. 1330–1342. DOI: https://doi.org/10.1161/CIRCULATIONAHA.117.031947

14. Gigli M., Merlo M., Graw S.L., et al. Genetic risk of arrhythmic phenotypes in patients with dilated cardiomyopathy // J Am Coll Cardiol. 2019. Vol. 74. P. 1480–1490. DOI: https://doi.org/10.1016/j.jacc.2019.06.072

15. Arbelo E., Protonotarios A., Gimeno J.R., et al. 2023 ESC Guidelines for the management of cardiomyopathies // European Heart Journal. 2023. Vol. 44, No. 37. P. 1–124. DOI: https://doi.org/10.1093/eurheartj/ehad194

16. Iles L.M., Ellims A.H., Llewellyn H., et al. Histological validation of cardiac magnetic resonance analysis of regional

and diffuse interstitial myocardial fibrosis // European Heart Journal–Cardiovascular Imaging. 2015. Vol. 16. P. 14–22. DOI: https://doi.org/10.1093/ehjci/jeu182

17. Olivas-Chacon C.I., Mullins C., Stewart K., et al. Magnetic Resonance Imaging of Non-ischemic Cardiomyopathies: A Pictorial Essay // Pictorial Essay. 2015. Vol. 5. P. 37. DOI: https://doi.org/10.4103/2156-7514.159564

18. Di Marco A., Anguera I., Schmitt M., et al. Late gadolinium enhancement and the risk for ventricular arrhythmias or sudden death in dilated cardiomyopathy: systematic review and meta-analysis // JACC Heart Fail. 2017. Vol. 5. P. 28–38. DOI: https://doi.org/10.1016/j.jchf.2016.09.017

19. Klem I., Klein M., Khan M., et al. Relationship of LVEF and myocardial scar to long-term mortality risk and mode of death in patients with nonischemic cardiomyopathy // Circulation. 2021. Vol. 143. P. 1343–1358. DOI: https://doi.org/10.1161/CIRCULATIONAHA.120.048477

20. Goidescu C.M. Dilated cardiomyopathy produced by lamin A/C gene mutations // Cluju Med. 2013. Vol. 86(4). P. 309–312.

21. Connolly S.J., Dorian P., Roberts R.S., et al. Comparison of beta-blockers, amiodarone plus beta-blockers, or sotalol for prevention of shocks from implantable cardioverter defibrillators: the OPTIC Study: a randomized trial // JAMA. 2006. Vol. 295. P. 165–171. DOI: https://doi.org/10.1001/jama.295.2.165

22. Dinov B., Fiedler L., Schönbauer R., et al. Outcomes in catheter ablation of ventricular tachycardia in dilated nonischemic cardiomyopathy compared with ischemic cardiomyopathy: results from the Prospective Heart Centre of Leipzig VT (HELP-VT) Study // Circulation. 2014. Vol. 129. P. 728–736. DOI: https://doi.org/10.1161/CIRCULATIONAHA.113.003063

23. Muser D., Santangeli P., Castro S.A., et al. Long-term outcome after catheter ablation of ventricular tachycardia in patients with nonischemic dilated cardiomyopathy // Circ. Arrhythm. Electrophysiol. 2016. Vol. 9. e004328. DOI: https://doi.org/10.1161/CIRCEP.116.004328

24. Ebert M., Richter S., Dinov B., et al. Evaluation and management of ventricular tachycardia in patients with dilated cardiomyopathy // Heart Rhythm. 2019. Vol. 16. P. 624–631. DOI: https://doi.org/10.1016/j.hrthm.2018.10.028

25. Kumar S., Androulakis A.F.A., Sellal J-M., et al. Multicenter experience with catheter ablation for ventricular tachycardia in lamin A/C cardiomyopathy // Circ Arrhythm Electrophysiol. 2016. Vol. 9. e004357. DOI: https://doi.org/10.1161/CIRCEP.116.004357

26. Oloriz T., Silberbauer J., Maccabelli G., et al. Catheter ablation of ventricular arrhythmia in nonischemic cardiomyopathy: anteroseptal versus inferolateral scar subtypes // Circ Arrhythm Electrophysiol. 2014. Vol. 7. P. 414–423. DOI: https://doi.org/10.1161/CIRCEP.114.001568

27. Corrado D., Link M.S., Calkins H. Arrhythmogenic right ventricular cardiomyopathy // N Engl J Med. 2017. Vol. 376. P. 1489–1490. DOI: https://doi.org/10.1056/NEJMra1509267

28. Corrado D., Marra M.P., Zorzi A., et al. Diagnosis of arrhythmogenic cardiomyopathy: The Padua criteria // Int J Cardiol. 2020. Vol. 319. P. 106–114. DOI: https://doi.org/10.1016/j.ijcard.2020.06.005.

29. Mazzanti A., Ng K., Faragli A., et al. Arrhythmogenic right ventricular cardiomyopathy: clinical course and predictors of arrhythmic risk // J Am Coll Cardiol. 2016. Vol. 68. P. 2540–2550. DOI: https://doi.org/10.1016/j.jacc.2016.09.951

30. Bhonsale A., Groeneweg J.A., James C.A., et al. Impact of genotype on clinical course in arrhythmogenic right ventricular dysplasia/cardiomyopathy-associated mutation carriers // Eur Heart J. 2015. Vol. 36. P. 847–855. DOI: https://doi.org/10.1093/eurheartj/ehu509

31. Rigato I., Bauce B., Rampazzo A., et al. Compound and digenic heterozygosity predicts life time arrhythmic outcome and sudden cardiac death in desmosomal gene-related arrhythmogenic right ventricular cardiomyopathy // Circ Cardiovasc Genet. 2013. Vol. 6. P. 533–542. DOI: https://doi.org/10.1161/CIRCGENETICS.113.000288

32. Novikova T.N., Novikov V.I., Sayganov S.A., Shcherbakova V.A. 2022 Esc guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: what is new? // Cardiac Arrhythmias. 2022. Vol. 2 (3). P. 7–30. DOI: https://doi.org/10.17816/cardar110961

33. Hulot J.-S., Jouven X., Empana J.-P., et al. Natural history and risk stratification of arrhythmogenic right ventricular dysplasia/cardiomyopathy // Circulation. 2004. Vol. 110. P. 1879–1884. DOI: https://doi.org/10.1161 /01.CIR.0000143375.93288.82

34. Wang W., Cadrin-Tourigny J., Bhonsale A., et al. Arrhythmic outcome of arrhythmogenic right ventricular cardiomyopathy patients without implantable defibrillators // J Cardiovasc Electrophysiol. 2018. Vol. 29. P. 1396–1402. DOI: https://doi.org/10.1111/jce.13668

35. Pinamonti B., Dragos A.M., Pyxaras S.A., et al. Prognostic predictors in arrhythmogenic right ventricular cardiomyopathy: results from a 10-year registry // Eur Heart J. 2011. Vol. 32. P. 1105–1113. DOI: https://doi.org/10.1093/eurheartj/ehr040

36. Brun F., Groeneweg J.A., Gear K., et al. Risk stratification in arrhythmic right ventricular cardiomyopathy without implantable cardioverter-defibrillators // JACC Clin Electrophysiol. 2016. Vol. 2. P. 558–564. DOI: https://doi.org/10.1016/j.jacep.2016.03.015

37. Bhonsale A., James C.A., Tichnell C., et al. Incidence and predictors of implantable cardioverter-defibrillator therapy in patients with arrhythmogenic right ventricular dysplasia/cardiomyopathy undergoing implantable cardioverter-defibrillator implantation for primary prevention // J Am Coll Cardiol. 2011. Vol. 58. P. 1485–1496. DOI: https://doi.org/10.1016/j.jacc.2011.06.043

38. Corrado D., Calkins H., Link M.S., et al. Prophylactic implantable defibrillator in patients with arrhythmogenic right ventricular cardiomyopathy/dysplasia and no prior ventricular fibrillation or sustained ventricular tachycardia // Circulation. 2010. Vol. 122. P. 1144–1152. DOI: https://doi.org/10.1161/CIRCULATIONAHA.109.913871

39. Platonov P.G., Haugaa K.H., Bundgaard H., et al. Primary prevention of sudden cardiac death with implantable cardioverter-defibrillator therapy in patients with arrhythmogenic right ventricular cardiomyopathy // Am J Cardiol. 2019. Vol. 123. P. 1156–1162. DOI: https://doi.org/10.1016/j.amjcard.2018.12.049

40. Link M.S., Laidlaw D., Polonsky B., et al. Ventricular arrhythmias in the North American multidisciplinary study of ARVC: predictors, characteristics, and treatment // J Am Coll Cardiol. 2014. Vol. 64. P. 119–125. DOI: https://doi.org/10.1016/j.jacc.2014.04.035

41. Cadrin-Tourigny J., Bosman L.P., Nozza A., et al. A new prediction model for ventricular arrhythmias in arrhythmogenic right ventricular cardiomyopathy // Eur Heart J. 2019. Vol. 40. P. 1850–1858. DOI: https://doi.org/10.1093/eurheartj/ehz103

42. Cadrin-Tourigny J., Bosman L.P., Wang W., et al. Sudden cardiac death prediction in arrhythmogenic right ventricular cardiomyopathy:

a multinational collaboration // Circ Arrhythm Electrophysiol. 2021. Vol. 14. e008509. DOI: https://doi.org/10.1161/CIRCEP.120.008509

43. Wichter T., Borggrefe M., Haverkamp W., et al. Efficacy of antiarrhythmic drugs in patients with arrhythmogenic right ventricular disease. Results in patients with inducible and noninducible ventricular tachycardia // Circulation. 1992. Vol. 86. P. 29–37. DOI: https://doi.org/10.1161/01.cir.86.1.29

44. Marcus G.M., Glidden D.V., Polonsky B., et al. Efficacy of antiarrhythmic drugs in arrhythmogenic right ventricular cardiomyopathy: a report from the North American ARVC Registry // J Am Coll Cardiol. 2009. Vol. 54. P. 609–615. DOI: https://doi.org/10.1016/j.jacc.2009.04.052

45. Mahida S., Venlet J., Saguner A.M., et al. Ablation compared with drug therapy for recurrent ventricular tachycardia in arrhythmogenic right ventricular cardiomyopathy: results from a multicenter study // Heart Rhythm. 2019. Vol. 16. P. 536–543. DOI: https://doi.org/10.1016/j.hrthm.2018.10.016

46. Ermakov S., Gerstenfeld E.P., Svetlichnaya Y., Scheinman M.M. Use of flecainide in combination antiarrhythmic therapy in patients with arrhythmogenic right ventricular cardiomyopathy // Heart Rhythm. 2017. Vol. 14. P. 564–569. DOI: https://doi.org/10.1016/j.hrthm.2016.12.010

47. Santangeli P., Zado E.S., Supple G.E., et al. Long-term outcome with catheter ablation of ventricular tachycardia in patients with arrhythmogenic right ventricular cardiomyopathy // Circ Arrhythm Electrophysiol. 2015. Vol. 8. P. 1413–1421. DOI: https://doi.org/10.1161/CIRCEP.115.003562

48. Ommen S.R., Mital S., Burke M.A., et al. 2020 AHA/ACC guideline for the diagnosis and treatment of patients with hypertrophic cardiomyopathy: executive summary: a report of the American College of Cardiology / American Heart Association Joint Committee on Clinical Practice Guidelines // Circulation. 2020. Vol. 142. e533–e557. DOI: https://doi.org/10.1161/CIR.0000000000000938

49. Heliö T., Elliott P., Koskenvuo J.W., et al. ESC EORP cardiomyopathy registry: real-life practice of genetic counselling and testing in adult cardiomyopathy patients // ESC Heart Fail. 2020. Vol. 7. P. 3013–3021. DOI: https://doi.org/10.1002/ehf2.12925

50. Ho C.Y., Day S.M., Ashley E.A., et al. Genotype and life time burden of disease in hypertrophic cardiomyopathy: insights from the Sarcomeric Human Cardiomyopathy Registry (SHaRe) // Circulation. 2018. Vol. 138. P. 1387–1398. DOI: https://doi.org/10.1161/CIRCULATIONAHA.117.033200

51. Semsarian C., Ingles J., Maron M.S., Maron B.J. New perspectives on the prevalence of hypertrophic cardiomyopathy // J Am Coll Cardiol. 2015. Vol. 65. P. 1249–1254. DOI: https://doi.org/10.1016/j.jacc.2015.01.019

52. Maron B.J., Rowin E.J., Casey S.A., et al. Hypertrophic cardiomyopathy in adulthood as sociated with low cardiovascular mortality with contemporary management strategies // J Am Coll Cardiol. 2015. Vol. 65. P. 1915–1928. DOI: https://doi.org/10.1016/j.jacc.2015.02.061

53. O'Mahony C., Jichi F., Pavlou M., et al. A novel clinical risk prediction model for sudden cardiac death in hypertrophic cardiomyopathy (HCMrisk-SCD) // Eur Heart J. 2014. Vol. 35. P. 2010–2020. DOI: https://doi.org/10.1093/eurheartj/eht439

54. O'Mahony C., Jichi F., Ommen S.R., et al. International External Validation Study of the 2014 European Society of Cardiology Guidelines on Sudden Cardiac Death Prevention in Hypertrophic Cardiomyopathy (EVIDENCE-HCM) // Circulation. 2018. Vol. 137. P. 1015–1023. DOI: https://doi.org/10.1161/CIRCULATIONAHA.117.030437

55. Vriesendorp P.A., Schinkel A.F.L., Liebregts M., et al. Validation of the 2014 European Society of Cardiology guidelines risk prediction model for the primary revention of sudden cardiac death in hypertrophic cardiomyopathy // Circ Arrhythm Electrophysiol. 2015. Vol. 8. P. 829–835. DOI: https://doi.org/10.1161/CIRCEP.114.002553

56. Lorenzini M., Anastasiou Z., O'Mahony C., et al. Mortality among referral patients with hypertrophic cardiomyopathy vs the general European population // JAMA Cardiol. 2020. Vol. 5. P. 73–80. DOI: https://doi.org/10.1001/jamacardio.2019.4534

57. Gimeno J.R., Tomé-Esteban M., Lofiego C., et al. Exercise-induced ventricular arrhythmias and risk of sudden cardiac death in patients with hypertrophic cardiomyopathy // Eur Heart J. 2009. Vol. 30. P. 2599–2605. DOI: https://doi.org/10.1093/eurheartj/ehp327

58. Norrish G., Qu C., Field E., et al. External validation of the HCM Risk-Kids model for predicting sudden cardiac death in childhood hypertrophic cardiomyopathy // Eur J Prev Cardiol. 2022. Vol. 29. P. 678–686. DOI: https://doi.org/10.1093/eurjpc/zwab181

59. Chan R.H., Maron B.J., Olivotto I., et al. Prognostic value of quantitative contrast-enhanced cardiovascular magnetic resonance for the evaluation of sudden death risk in patients with hypertrophic cardiomyopathy // Circulation. 2014. Vol. 130. P. 484–495. DOI: https://doi.org/10.1161/CIRCULATIONAHA.113.007094

60. He D., Ye M., Zhang L., Jiang B. Prognostic significance of late gadolinium enhancement on cardiac magnetic resonance in patients with hypertrophic cardiomyopathy // Heart Lung. 2018. Vol. 47. P. 122–126. DOI: https://doi.org/10.1016/j.hrtlng.2017.10.008

61. Rowin E.J., Maron B.J., Carrick R.T., et al. Outcomes in patients with hypertrophic cardiomyopathy and left ventricular systolic dysfunction // J Am Coll Cardiol. 2020. Vol. 75. P. 3033–3043. DOI: https://doi.org/10.1016/j.jacc.2020.04.045

62. Rowin E.J., Maron B.J., Haas T.S., et al. Hypertrophic cardiomyopathy with left ventricular apical aneurysm: implications for risk stratification and management // J Am Coll Cardiol. 2017. Vol. 69. P. 761–773. DOI: https://doi.org/10.1016/j.jacc.2016.11.063

63. Sadoul N., Prasad K., Elliott P.M., et al. Prospective prognostic assessment of blood pressure response during exercise in patients with hypertrophic cardiomyopathy // Circulation. 1997. Vol. 96. P. 2987–2991. DOI: https://doi.org/10.1161/01.cir.96.9.2987

64. Elliott P.M., Poloniecki J., Dickie S., et al. Sudden death in hypertrophic cardiomyopathy: identification of high risk patients // J Am Coll Cardiol. 2000. Vol. 36. P. 2212–2218. DOI: https://doi.org/10.1016/s0735-1097(00)01003-2

65. Behr E.R., Elliott P., McKenna W.J. Role of invasive EP testing in the evaluation and management of hypertrophic cardiomyopathy // Card Electrophysiol Rev. 2002. Vol. 6. P. 482–486. DOI: https://doi.org/10.1023/a:1021161114347

66. Gatzoulis K.A., Georgopoulos S., Antoniou C.-K., et al. Programmed ventricular stimulation predicts arrhythmic events and survival in hypertrophic cardiomyopathy // Int J Cardiol. 2018. Vol. 254. P. 175–181. DOI: https://doi.org/10.1016/j.ijcard.2017.10.033

67. Elliott P.M., Sharma S., Varnava A., et al. Survival after cardiac arrest or sustained ventricular tachycardia in patients with

hypertrophic cardiomyopathy // J Am Coll Cardiol. 1999. Vol. 33. P. 1596–1601. DOI: https://doi.org/10.1016/s0735-1097(99)00056-x

68. Cecchi F., Maron B.J., Epstein S.E. Long-term outcome of patients with hypertrophic cardiomyopathy successfully resuscitated after cardiac arrest // J Am Coll Cardiol. 1989. Vol. 13. P. 1283–1288. DOI: https://doi.org/10.1016/0735-1097(89)90302-1

69. Maron B.J., Spirito P., Shen W-K., et al. Implantable cardioverter-defibrillators and prevention of sudden cardiac death in hypertrophic cardiomyopathy // JAMA. 2007. Vol. 298. P. 405–412. DOI: https://doi.org/10.1001/jama.298.4.405

70. Link M.S., Bockstall K., Weinstock J., et al. Ventricular tachyarrhythmias in patients with hypertrophic cardiomyopathy and defibrillators: triggers, treatment, and implications // J Cardiovasc Electrophysiol. 2017. Vol. 28. P. 531–537. DOI: https://doi.org/10.1111/jce.13194

71. Dallaglio P.D., DiMarco A., MorenoWeidmann Z., et al. Antitachycardia pacing for shock prevention in patients with hypertrophic cardiomyopathy and ventricular tachycardia // Heart Rhythm. 2020. Vol. 17. P. 1084–1091. DOI: https://doi.org/10.1016/j.hrthm.2020.02.024

72. Adduci C., Semprini L., Palano F., et al. Safety and efficacy of anti-tachycardia pacing in patients with hypertrophic cardiomyopathy implanted with an ICD // Pacing Clin Electrophysiol. 2019. Vol. 42. P. 610–616. DOI: https://doi.org/10.1111/pace.13665

73. Melacini P., Maron B.J., Bobbo F., et al. Evidence that pharmacological strategies lack efficacy for the prevention of sudden death in hypertrophic cardiomyopathy // Heart. 2007. Vol. 93. P. 708–710. DOI: https://doi.org/10.1136/hrt.2006.099416

74. McKenna W.J., Oakley C.M., Krikler D.M., Goodwin J.F. Improved survival with amiodarone in patients with hypertrophic cardiomyopathy and ventricular tachycardia // Br Heart J. 1985. Vol. 53. P. 412–416. DOI: https://doi.org/10.1136/hrt.53.4.412

75. Vaseghi M., Hu T.Y., Tung R., et al. Outcomes of catheter ablation of ventricular tachycardia based on etiology in nonischemic heart disease: an international ventricular tachycardia ablation center collaborative study // JACC Clin Electrophysiol. 2018. Vol. 4. P. 1141–1150. DOI: https://doi.org/10.1016/j.jacep.2018.05.007

76. Igarashi M., Nogami A., Kurosaki K., et al. Radiofrequency catheter ablation of ventricular tachycardia in patients with hypertrophic cardiomyopathy and apical aneurysm // JACC Clin Electrophysiol. 2018. Vol. 4. P. 339–350. DOI: https://doi.org/10.1016/j.jacep.2017.12.020

77. Dukkipati S.R., d'Avila A., Soejima K., et al. Long-term outcomes of combined epicardial and endocardial ablation of monomorphic ventricular tachycardia related to hypertrophic cardiomyopathy // Circ Arrhythm Electrophysiol. 2011. Vol. 4. P. 185–194. DOI: https://doi.org/10.1161/CIRCEP.110.957290

78. Новиков В.И. Кардиомиопатии / В.И. Новиков, Т.Н. Новикова. Москва: МЕДпресс-информ, 2021. 112 с.ISBN 978-5-00030-850-9

79. Towbin J.A., Lorts A., Jefferies J.L. Left ventricular non-compaction cardiomyopathy // Lancet. 2015. Vol. 386(9995). P. 813-25. DOI: https://doi.org/10.1016/S0140-6736(14)61282-4

80. Gerecke B.J., Engberding R. Noncompaction Cardiomyopathy – History and Current Knowledge for Clinical Practice // J Clin Med. 2021. Vol. 10(11). P. 2457. DOI: https://doi.org/10.3390/jcm10112457

81. Aung N., Doimo S., Ricci F., et al. Prognostic significance of left ventricular noncompaction: systematic review and meta-analysis of observational studies // Circ Cardiovasc Imaging. 2020. Vol. 13. e009712. DOI: https://doi.org/10.1161/CIRCIMAGING.119.009712

82. Grigoratos C., Barison A., Ivanov A., et al. Meta-analysis of the prognostic role of late gadolinium enhancement and global systolic impairment in left ventricular noncompaction // JACC Cardiovasc Imaging. 2019. Vol. 12. P. 2141–2151. DOI: https://doi.org/10.1016/j.jcmg.2018.12.029

83. Richard P., Ader F., Roux M., et al. Targeted panel sequencing in adult patients with left ventricular non-compaction reveals a large genetic heterogeneity // Clin Genet. 2019. Vol. 95. P. 356–367. DOI: https://doi.org/10.1111/cge.13484

84. Baig S., Edward N.C., Kotecha D., et al. Ventricular arrhythmia and sudden cardiac death in Fabry disease: a systematic review of risk factors in clinical practice // Europace 2018. Vol. 20. f153–f161. DOI: https://doi.org/10.1093/europace/eux261

AUTHORS INFO

***Tatiana N. Novikova,** Cand. Sci. (Med.), associate professor of the Department of Hospital Therapy and Cardiology named after M.S. Kushakovskiy. North-Western State Medical University named after I.I. Mechnikov, Saint Petersburg;
ORCID: 0000-0003-4655-0297; eLibrary SPIN: 3401-0329;
e-mail: novikova-tn@mail.ru

Fatima I. Bitakova, Cand. Sci. (Med.), associate professor;
ORCID: 0000-0001-6637-8266; eLibrary SPIN: 8624-7193;
e-mail: Fatima.Bitakova@szgmu.ru

Valeria S. Ignateva, 6th year student;
ORCID: 0009-0008-9446-9374; e-mail: valeria2311@bk.ru

ОБ АВТОРАХ

***Татьяна Николаевна Новикова,** канд. мед. наук, доцент кафедры госпитальной терапии и кардиологии им. М.С. Кушаковского Северо-Западного государственного медицинского университета имени И.И. Мечникова, Санкт-Петербург;
ORCID: 0000-0003-4655-0297; eLibrary SPIN: 3401-0329;
e-mail: novikova-tn@mail.ru

Фатима Измаиловна Битакова, канд. мед. наук, доцент;
ORCID: 0000-0001-6637-8266; eLibrary SPIN: 8624-7193;
e-mail: Fatima.Bitakova@szgmu.ru

Валерия Семёновна Игнатьева, студентка 6 курса;
ORCID: 0009-0008-9446-9374; e-mail: valeria2311@bk.ru

* Corresponding author / Автор, ответственный за переписку

Vladimir I. Novikov, Dr. Sci. (Med.), professor;
ORCID: 0000-0002-2493-6300; eLibrary SPIN: 6909-3377;
e-mail: novikov-vi@mail.ru

Sergey A. Sayganov, Dr. Sci. (Med.), professor, rector;
ORCID: 0000-0001-8325-1937; eLibrary SPIN: 2174-6400;
e-mail: sergey.sayganov@szgmu.ru

Vladislava A. Shcherbakova, 6th year student;
e-mail: shcher.vl@yandex.ru

Владимир Игоревич Новиков, д-р мед. наук, профессор;
ORCID: 0000-0002-2493-6300; eLibrary SPIN: 6909-3377;
e-mail: novikov-vi@mail.ru

Сергей Анатольевич Сайганов, д-р мед. наук, профессор, ректор; ORCID: 0000-0001-8325-1937; eLibrary SPIN: 2174-6400;
e-mail: sergey.sayganov@szgmu.ru

Владислава Александровна Щербакова, студентка 6 курса;
e-mail: shcher.vl@yandex.ru