

VOLUME 4

ISSUE 3

2024

Cardiac Arrhythmias

INTERNATIONAL PEER-REVIEW MEDICAL JOURNAL

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







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Eco-Vector Address:

3A Aptekarskiy lane, office 1N, Saint Petersburg, 191181, 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 № ФС 77-79865

Published quarterly

EDITORIAL OFFICE

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

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INDEXATION

- Russian Index of Science Citation
- Dimensions
- Scilit
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SUBSCRIPTION

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



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

CARDIAC ARRHYTHMIAS

Volume 4 | Issue 3 | 2024

INTERNATIONAL PEER-REVIEW MEDICAL JOURNAL

Published under the supervision of Eurasian Arrhythmology Association

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Журнал зарегистрирован Федеральной службой по надзору в сфере массовых коммуникаций, связи и охраны культурного наследия, свидетельство о регистрации СМИ ПИ № ФС 77–79865 от 18.12.2020

Выходит 4 раза в год

РЕДАКЦИЯ

191015, Санкт-Петербург, ул. Кирочная, д. 41 Тел.: +7(812)303-50-00 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/cardar

OPEN ACCESS

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

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подготовлен в издательстве «Эко-Вектор». Редактор переводческих проектов: Е.О. Кондратьева Выпускающий редактор: Н.Н. Репьева Корректор: И.В. Смирнова Верстка: А.Г. Хуторовская

Формат $60 \times 90^{1}/_{8}$. Печать офсетная. Усл. печ. л. 5. Тираж 200 экз. Цена свободная.

Отпечатано в 000 «Типография Экспресс B2B». 191180, Санкт-Петербург, наб. Реки Фонтанки, д. 104, лит. А, пом. 3H, оф. 1. Тел.: +7(812)646-33-77.

Заказ № 5-4062-lv. Подписано в печать: 17.03.2025. Выход в свет: 21.03.2025.

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

CARDIAC ARRHYTHMIAS

Том 4 | Выпуск 3 | 2024

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DOI: https://doi.org/10.17816/cardar643257

2024 European Society of Cardiology Guidelines for the management of atrial fibrillation, developed in collaboration with the European Association for Cardio-Thoracic Surgery: what's new?

Tatiana N. Novikova, Danila A. Kunshin, Irina A. Dolinina, Lyubov S. Dyatchina, Fatima I. Bitakova, Vladimir I. Novikov, Sergey A. Sayganov

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ABSTRACT

The article presents key approaches to the diagnosis and treatment of atrial fibrillation in light of the new 2024 ESC Guidelines for the management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery. The main changes made to the new recommendations are reflected. The innovative patient-oriented principle of atrial fibrillation treatment — AF-CARE is considered in detail. An analysis of the updated scale for assessing the risk of stroke and systemic embolism CHA2DS2-VA is given. The article provides definitions of clinical, subclinical, trigger-induced, newly diagnosed, paroxysmal, persistent and permanent forms of atrial fibrillation, algorithms for the treatment of different forms of atrial fibrillation based on the choice of drug therapy taking into account the left ventricular ejection fraction. Much attention is paid to screening and early detection of atrial fibrillation. The categories of patients for whom screening is advisable are determined. The importance of early diagnostics of atrial cardiomyopathy using atrial myocardial strain analysis is emphasized. The role of timely, guideline-based treatment of comorbid pathology such as chronic heart failure, diabetes mellitus, obesity, obstructive sleep apnea, arterial hypertension and others is emphasized in order to prevent atrial fibrillation and, if it occurs, to reduce relapses.

Keywords: atrial fibrillation; sinus rhythm control; ventricular rate control; stroke prevention.

To cite this article

Novikova TN, Kunshin DA, Dolinina IA, Dyatchina LS, Bitakova FI, Novikov VI, Sayganov SA. 2024 European Society of Cardiology Guidelines for the management of atrial fibrillation, developed in collaboration with the European Association for Cardio-Thoracic Surgery: what's new? *Cardiac Arrhythmias*. 2024;4(3):5–14. DOI: https://doi.org/10.17816/cardar643257

Received: 20.12.2024 Accepted: 20.01.2025 Published online: 15.02.2025



HAYYHBIE 0Б30Pbl Tom 4, № 3, 2024 Cardiac Arrhythmias

DOI: https://doi.org/10.17816/cardar643257

Рекомендации Европейского общества кардиологов 2024 по лечению фибрилляции предсердий, разработанные в содружестве с Европейской ассоциацией кардиоторакальных хирургов: что нового?

Т.Н. Новикова, Д.А. Куншин, И.А. Долинина, Л.С. Дятчина, Ф.И. Битакова, В.И. Новиков, С.А. Сайганов

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В статье представлены ключевые подходы к диагностике и лечению фибрилляции предсердий в свете новых Рекомендаций Европейского общества кардиологов 2024 г. по лечению фибрилляции предсердий, разработанных в содружестве с Европейской ассоциацией кардиоторакальных хирургов. Отражены основные изменения, внесенные в новые рекомендации. Подробно рассмотрен инновационный пациенториентированный принцип лечения фибрилляции предсердий — AF-CARE. Дан анализ обновлённой шкалы оценки риска инсульта и системных эмболий CHA2DS2-VA. Приведены определения клинической, субклинической, триггер-индуцированной, впервые выявленной, пароксизмальной, персистирующей и постоянной форм фибрилляции предсердий, алгоритмы лечения разных форм фибрилляции предсердий, основанные на выборе медикаментозной терапии с учётом фракции выброса левого желудочка. Большое внимание уделено скринингу и раннему выявлению фибрилляции предсердий. Определены категории пациентов, у которых целесообразно проводить скрининг. Подчёркнута важность ранней диагностики предсердной кардиомиопатии с помощью анализа деформации миокарда предсердий. Сделан акцент на роли своевременного, базирующегося на актуальных рекомендациях лечения коморбидной патологии, такой как хроническая сердечная недостаточность, сахарный диабет, ожирение, обструктивное апноэ сна, артериальная гипертензия и других, с целью профилактики фибрилляции предсердий, а при ее появлении — уменьшения рецидивов.

Ключевые слова: фибрилляция предсердий; контроль синусового ритма; контроль частоты желудочковых сокращений; профилактика инсульта.

Как цитировать

Новикова Т.Н., Куншин Д.А., Долинина И.А., Дятчина Л.С., Битакова Ф.И., Новиков В.И., Сайганов С.А. Рекомендации Европейского общества кардиологов 2024 по лечению фибрилляции предсердий, разработанные в содружестве с Европейской ассоциацией кардиоторакальных хирургов: что нового? // Cardiac Arrhythmias. 2024. Т. 4, № 3. С. 5—14. DOI: https://doi.org/10.17816/cardar643257

Рукопись получена: 20.12.2024 Рукопись одобрена: 20.01.2025 Опубликована online: 15.02.2025



INTRODUCTION

Atrial fibrillation (AF) is one of the most commonly encountered arrhythmias. According to the 2024 European Society of Cardiology Guidelines for the management of atrial fibrillation, the current prevalence of AF is estimated at 1%–2% of the general population [1]. Similar figures are reported in the 2020 national guidelines for the diagnosis and treatment of atrial fibrillation and atrial flutter [2]. Some publications even suggest higher prevalence of AF [3–5]. It is expected that the prevalence of AF will double in the coming decades, driven by population aging, the growing burden of comorbidities complicated by AF, increased patient awareness, enhanced screening in high-risk groups, and advancements in technologies for detecting asymptomatic AF.

DEFINITION, DIAGNOSIS, CLASSIFICATION

AF is a supraventricular arrhythmia characterized by uncoordinated atrial activation and loss of effective atrial contraction [1]. On surface electrocardiogram (ECG), AF is identified by the absence of distinct *P* waves and the presence of irregular *QRS* complexes.

The diagnosis of AF in symptomatic patients is typically straightforward: the presence of characteristic symptoms combined with AF-specific findings on a standard 12-lead ECG allows for an accurate diagnosis. In asymptomatic patients, diagnosis is more challenging. In asymptomatic episodes detected using long-term monitoring devices, particularly those that do not record standard ECG signals (e.g., oscillometric, photoplethysmographic, mechanocardiographic), AF should be confirmed on a conventional ECG [1]. The confirmation may be made using a standard 12-lead ECG or devices capable of recording one or more ECG leads [1]. The minimum duration of an AF episode required for diagnosis remains undefined. The recording time for a standard 12-lead ECG is 10 s, whereas the 2020 guidelines contain a consensus statement that a AF episode lasting at least 30 s is necessary for diagnosis when using devices with one or more ECG leads [1]. The 2024 ESC guidelines do not specify a minimum duration for AF diagnosis.

In the 2024 ESC guidelines, the classification of AF remains unchanged. The following categories are still recognized:

- newly diagnosed AF (AF that has not been previously diagnosed, regardless of symptoms, temporal pattern, or duration);
- paroxysmal AF (AF that terminates spontaneously or with medical intervention within 7 days of onset, with most spontaneous conversions to sinus rhythm occurring within the first 48 h) [6];
- persistent AF (AF episodes that do not terminate spontaneously within 7 days, long-standing persistent AF is defined as continuous AF lasting at least 12 months;

however, rhythm control remains a treatment option, distinguishing this form from permanent AF) [7, 8];

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 permanent AF (AF in which no further attempts to restore sinus rhythm are planned, based on shared decisionmaking between a patient and a physician).

The definition of clinical AF has been slightly modified: it now refers to symptomatic or asymptomatic AF that is clearly documented by a physician using ECG (either a standard 12-lead ECG or a high-quality ECG recorded by other devices). The minimum duration required to diagnose clinical AF remains unclear and depends on the clinical context. Episodes lasting ≥30 s may indicate the clinical significance of arrhythmia, necessitating further monitoring of the patient and their arrhythmia, as well as risk stratification for thromboembolism and prevention of thromboembolic events.

With the increasing implementation of screening for early detection of asymptomatic AF, the term device-detected subclinical AF has been introduced. This refers to subclinical asymptomatic AF detected using devices such as implanted cardiac electronic devices, consumer wearable monitors, and others. Most atrial high-rate episodes recorded by devices (≥170 bpm, lasting >5 min) may represent AF [1]. All episodes of atrial high-rate activity must be visually reviewed by a physician, as some may be electrical artifacts, creating a false impression of AF. Confirmation by a competent specialist capable of interpreting intracardiac electrograms or ECG recordings from consumer devices is essential [9, 10]. Device-detected subclinical AF is a predictor of future clinical AF [11]. Currently, there is no clear consensus on whether subclinical AF should be treated. However, patients with subclinical AF require monitoring and management of risk factors that may contribute to its progression to clinical AF. Screening using 24-hour ECG monitoring is recommended for patients aged ≥75 years or those aged ≥65 years with additional risk factors based on the CHA2DS2-VA score, to ensure earlier detection of AF (Class IIa, Level B).

A new category, trigger-induced AF, has been introduced, which is defined as a new AF episode occurring in close proximity to a triggering and potentially reversible factor [12–15].

AF is fundamentally driven by atrial cardiomyopathy, which is defined as a combination of structural, electrical, or functional changes in the atria that lead to clinical sequelae, such as AF progression/recurrence, limited efficacy of AF therapy, and/or the development of heart failure [16, 17]. Atrial cardiomyopathy involves inflammatory and prothrombotic atrial remodeling, neurohormonal activation, and myocardial fibrosis [18]. In our view, besides volumetric characteristics, the assessment of atrial remodeling should include the analysis of atrial myocardial strain [19, 20].

AF-CARE PRINCIPLES

The AF-CARE principles have replaced the ABC approach in the management of AF patients. In the acronym

AF-CARE, C stands for Comorbidity and risk factor management, A for Avoid stroke and thromboembolism, R for Reduce symptoms by rate and rhythm control, E for Evaluation and dynamic reassessment [1]. The approach is focused on AF prevention, early arrhythmia detection, and a multidisciplinary, personalized patient management strategy. The control of risk factors such as poor diet, excessive alcohol consumption, obesity, smoking, drug use, low physical activity, and a sedentary lifestyle is deemed crucial. A key role of timely, guideline-based management of comorbidities, including chronic heart failure (CHF), diabetes mellitus, obesity, obstructive sleep apnea, and hypertension, is emphasized to prevent AF and, in diagnosed cases, reduce recurrence.

STROKE AND SYSTEMIC THROMBOEMBOLISM PREVENTION

The risk assessment scale for stroke and systemic embolism has been revised. It has been proposed that female sex should no longer be considered an independent risk factor for thrombotic complications, as it serves as a stroke risk modifier dependent on age rather than an independent predictor [21-24]. In the previous 2020 ESC guidelines, as well as in the Russian national guidelines, female sex was formally included as a risk factor in the CHA2DS2-VASc score. Consequently, the indication for oral anticoagulants differed between men and women with AF, as women received an additional risk point based on sex under otherwise equal conditions. The newly introduced CHA2DS2-VA score no longer includes female sex as a thromboembolic risk factor. Regardless of sex, oral anticoagulants are recommended for patients with CHA_2DS_2 -VA ≥ 2 (Class I, Level C). For those with $CHA_2DS_2 = 1$, the use of oral anticoagulants should be considered (Class IIa Level C), taking into account additional thromboembolic risk modifiers. These include cancer, chronic kidney disease, ethnicity (Black, Latino, Asian), biomarkers (elevated troponin and natriuretic peptide levels), left atrial enlargement, hyperlipidemia, smoking, and obesity [1].

The acronym CHA₂DS₂-VA is defined as follows [1].

C for Chronic heart failure, 1 risk point. CHF is defined by the presence of symptoms and signs of CHF, regardless of left ventricular ejection fraction (LVEF), including heart failure with reduced ejection fraction (HFrEF), heart failure with mildly reduced ejection fraction (HFmrEF), heart failure with preserved ejection fraction (HFpEF), or asymptomatic LVEF \leq 40% [25–27].

H for Hypertension, 1 risk point. Hypertension is defined as resting blood pressure (BP) >140/90 mmHg in at least 2 measurements or current antihypertensive therapy to achieve target BP levels. The BP range associated with the lowest cardiovascular risk is 120–129/70–79 mmHg. If achieving target values is not feasible, maintaining BP at the lowest reasonable level is recommended [28, 29].

 A_2 for Age \geqslant 75 years, 2 risk points. Age is an independent risk factor for ischemic stroke [30]. Although stroke risk increases along a continuum with age, for practical purposes, patients aged \geqslant 75 years receive a score of 2.

D for Diabetes mellitus, 1 risk point. Diabetes mellitus is defined as type 1 or type 2 diabetes diagnosed according to current criteria or requiring glucose-lowering therapy [31].

 $\rm S_2$ for Prior Stroke, transient ischemic attack (TIA), or arterial thromboembolism, 2 risk points. A history of thromboembolic events is associated with a significantly increased risk of recurrence, warranting the assignment of 2 points.

V for Vascular disease, 1 risk point. The patient has confirmed coronary artery disease (CAD), including a history of myocardial infarction, angina, coronary revascularization (surgical or percutaneous), significant coronary artery disease on coronary angiography or other imaging studies [32], peripheral arterial disease (PAD) with intermittent claudication, prior peripheral arterial revascularization, percutaneous or surgical interventions on the abdominal aorta, or multiple aortic plaques identified on imaging (mobile, ulcerated, or ≥4 mm thick) [33, 34].

A for Age 65-74 years, 1 risk point.

During follow-up, periodic individualized reassessment of thromboembolic risk is recommended for patients with AF to ensure the timely initiation and adjustment of anticoagulant therapy.

The 2024 ESC guidelines identify two groups of patients who, due to their high risk of thromboembolic events, should receive oral anticoagulants chronically regardless of their CHA₂DS₂-VA score. In these patients, risk assessment is not required for anticoagulant prescription [35–41]. These groups include those with hypertrophic cardiomyopathy and those with amyloid cardiomyopathy

Direct oral anticoagulants (DOACs) are preferred over vitamin K antagonists (VKAs).

To prevent underdosing and ensure adequate drug concentrations for thromboembolic prevention, the guidelines emphasize that unjustified dose reductions of DOACs should be avoided unless the patient meets specific criteria for dose adjustment as per the drug's prescribing information.

The use of oral anticoagulants may be considered for patients with asymptomatic, device-detected subclinical AF and an increased risk of thromboembolic events to prevent ischemic stroke and systemic thromboembolism, except in those with a high bleeding risk (Class IIb, Level B) [1]. However, the guidelines emphasize that the AF burden required to initiate oral anticoagulant therapy remains unknown.

In patients with AF, the addition of antiplatelet agents to oral anticoagulant therapy for stroke prevention is not recommended. Similarly, switching from one DOAC to another or from a DOAC to a VKA for the prevention of recurrent thromboembolic events is not advised.

Long-term oral anticoagulant therapy should be considered for patients with trigger-induced AF and

an elevated thromboembolic risk to prevent ischemic stroke and thromboembolic complications (Class IIa, Level C).

At the start of antithrombotic therapy, its safety is essential. This requires the identification and correction of modifiable and partially modifiable risk factors for bleeding, including strict blood pressure control, reduction of excessive alcohol consumption, avoidance of antiplatelet agents and nonsteroidal or corticosteroid anti-inflammatory drugs, maintenance of an adequate time in the therapeutic range of the international normalized ratio when using VKAs, and assessment of drug interactions. Systematic reviews and validation studies evaluating the predictive value of various bleeding risk assessment scales have shown inconsistent results and only modest prognostic accuracy [42-51]. Consequently, the 2024 ESC guidelines do not refer to a single bleeding risk assessment scale due to the uncertainty in accurate risk assessment with any scale and the potential adverse consequences of withholding oral anticoagulants in patients at high risk of both thromboembolism and bleeding. Several bleeding risk assessment scales are presented, including ABC-bleeding, ATRIA, DOAC, GARFIELD-AF, HAS-BLED, HEMORR2HAGES, ORBIT. The guidelines emphasize that bleeding risk assessment scales should not be used as a single criterion for withholding or discontinuing anticoagulation therapy, as the risk of thrombotic complications in patients with AF generally outweighs the risk of bleeding [52, 53]. Physicians should carefully consider stroke and bleeding risks, as these factors are dynamic and interrelated, requiring reassessment at each patient visit with the elimination of modifiable risk factors whenever possible. Patients with nonmodifiable bleeding risk factors should be regularly monitored by a multidisciplinary team, including specialists in the management of relevant comorbid conditions.

REDUCTION OF SYMPTOMS THROUGH HEART RATE AND RHYTHM CONTROL

Newly Diagnosed Atrial Fibrillation

The guidelines provide a structured algorithm for managing patients with newly diagnosed AF [1]. The initial step is to determine whether the patient is hemodynamically stable or unstable. In cases of hemodynamic instability, urgent electrical cardioversion is indicated. In hemodynamically stable patients, management should follow the AF-CARE principles, including control of comorbid conditions and AF risk factors, prevention of stroke and systemic thromboembolic events, and initial heart rate (HR) control. The choice of initial HR control therapy, before establishing a long-term management strategy, depends on the LVEF. In patients with LVEF >40%, available pharmacologic options include β -blockers, digoxin, and non-dihydropyridine calcium channel blockers (diltiazem or verapamil) (Class I). If monotherapy fails to achieve target resting HR,

combination therapy with a β -blocker and digoxin or a non-dihydropyridine calcium channel blocker (diltiazem or verapamil) and digoxin may be considered (Class IIa). In patients with reduced LVEF (≤40%), non-dihydropyridine calcium channel blockers (diltiazem and verapamil) are contraindicated. The preferred agents for initial HR control in these patients are β-blockers and/or digoxin (Class I for monotherapy, Class IIa for combination therapy). For patients with symptomatic newly diagnosed AF and stable hemodynamics, elective cardioversion is recommended (Class I). A wait-and-see approach is recommended, as spontaneous restoration of sinus rhythm may occur within 48 h of AF onset (Class IIa). When planning early cardioversion, therapeutic-dose anticoagulation—using DOACs, VKAs, low-molecularweight heparin, or unfractionated heparin—should be initiated as soon as possible to prevent cardioversionrelated thromboembolism. Early cardioversion is not recommended without prior anticoagulation therapy for at least three weeks or transesophageal echocardiography to exclude left atrial thrombi before cardioversion if AF duration exceeds 24 h. Most patients should continue oral anticoagulation for at least 4 weeks after cardioversion. A novel approach to anticoagulation after cardioversion allows omitting anticoagulants in patients without thromboembolic risk factors if sinus rhythm is restored within 24 h of AF onset [1]. However, in the presence of any thromboembolic risk factors, long-term oral anticoagulation should be prescribed regardless of the cardioversion outcome.

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Management of Patients with Paroxysmal Atrial Fibrillation

In patients diagnosed with paroxysmal AF [1], strict adherence to all AF-CARE principles is essential.

During an AF episode, initial HR control in patients with a LVEF >40% is achieved using β -blockers, digoxin, or non-dihydropyridine calcium channel blockers (diltiazem or verapamil) (Class I). If monotherapy fails to achieve target resting HR, combination therapy with a β-blocker and digoxin or a non-dihydropyridine calcium channel blocker (diltiazem or verapamil) and digoxin may be considered (Class IIa). In patients with reduced LVEF (≤40%), β-blockers and/ or digoxin are the preferred options for initial HR control (Class I for monotherapy, Class IIa for combination therapy). The initial target HR is <110 bpm (lenient control) (Class IIa). If symptoms persist despite lenient HR control, a strict approach (<80 bpm) should be considered (Class IIa). Patients should actively participate in selecting the management strategy, and rhythm control decisions should be made jointly by the physician and the patient (Class I). The choice of antiarrhythmic drug depends on LVEF and comorbid conditions. For patients with HFrEF (LVEF ≤40%), amiodarone is the only recommended antiarrhythmic drug for rhythm

control (Class I). In patients with HFmrEF (LVEF 41%-49%), the 2024 ESC guidelines allow for a broader selection of drugs: amiodarone or dronedarone¹ (Class I), with sotalol as an alternative in cases of inefficacy, intolerance, or contraindications for these drugs (Class IIb). A similar approach is recommended for patients with CAD or valvular heart disease. In the absence of structural heart disease (lone AF) or minimal cardiac pathology, dronedarone, flecainide, or propafenone are recommended (Class I). If these are ineffective, poorly tolerated, or contraindicated, sotalol may be considered, albeit with a lower level of recommendation (Class IIb). If antiarrhythmic drug therapy is ineffective, the physician and patient may jointly decide on a catheter-based procedure to maintain sinus rhythm (Class I). If catheter ablation fails, several management options are available: repeating the catheter procedure (Class IIa), performing surgical or hybrid ablation (Class IIb), or continuing antiarrhythmic drug therapy.

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Management of Patients with Persistent Atrial Fibrillation

When managing patients with persistent AF, strict adherence to the AF-CARE principles is essential. However, the management approach [1] differs slightly from that used for patients with paroxysmal AF.

For initial HR control in patients with LVEF >40%, B-blockers, digoxin, or non-dihydropyridine calcium channel blockers (diltiazemor verapamil) are recommended (Class I). If monotherapy fails to achieve target resting HR, combination therapy with a β-blocker and digoxin or a non-dihydropyridine calcium channel blocker (diltiazem or verapamil) and digoxin may be considered (Class IIa). HR should be monitored to avoid bradycardia. In patients with reduced LVEF (≤40%), β-blockers and/or digoxin are the preferred options for initial HR control (Class I for monotherapy, Class IIa for combination therapy). The initial target resting HR is <110 bpm (lenient control, Class IIa). If symptoms persist despite the lenient control, a strict approach (<80 bpm) should be considered (Class IIa). The choice of AF management strategy should be made jointly by the physician and the patient (Class I). If there are clear clinical and historical benefits of maintaining sinus rhythm, rhythm control should be recommended (Class IIa). Either pharmacologic or catheter-based approaches may be considered as a first-line strategy (Class IIb for catheter ablation). The choice of antiarrhythmic drug depends on LVEF and the presence of comorbid conditions, similar to the approach in paroxysmal AF. In patients with HFrEF (LVEF ≤40%), amiodarone is the only recommended drug for rhythm control (Class I). In patients with HFmrEF (LVEF 41% to 49%), CAD, or valvular heart disease, amiodarone or dronedarone is recommended (Class I). If these drugs are ineffective, not tolerated, or contraindicated, sotalol

may be considered, but with a lower recommendation level (Class IIb). In patients with no structural heart disease (lone AF) or minimal cardiac pathology, dronedarone, flecainide, or propafenone is recommended (Class I). If these are ineffective, poorly tolerated, or contraindicated, sotalol may be considered, albeit with a lower level of recommendation (Class IIb). If AF recurs despite antiarrhythmic drug therapy, catheter ablation is recommended (Class I). Endoscopic or hybrid ablation may also be considered (Class IIa). If catheter ablation was used as a first-line strategy, several options exist for further management: repeat catheter ablation, perform endoscopic/hybrid/surgical ablation, continue antiarrhythmic drug therapy or accept a permanent AF strategy with rate control instead of pursuing sinus rhythm maintenance.

Management of Patients with Permanent Atrial Fibrillation [1]

The AF-CARE principles are fundamental in managing all forms of AF. Addressing risk factors, adequately treating comorbid conditions, and preventing thromboembolic events are cornerstones of patient management in permanent AF. In this setting, HR control is of paramount importance. The selection of medications for long-term rate control, whether monotherapy or combination therapy, follows the same principles as for newly diagnosed, paroxysmal, and persistent AF. If permanent AF with tachycardia is associated with severe symptoms and at least one hospitalization due to HF, atrioventricular node ablation with cardiac resynchronization therapy may be considered as a first-line strategy (Class IIa). Atrioventricular node ablation with pacemaker implantation should also be considered if target HR control cannot be achieved with medications (Class IIa). The choice of pacing modality (right ventricular or biventricular pacing) depends on patient characteristics, the presence of HF, and LVEF. To optimize outcomes, the pacemaker should be implanted several weeks before atrioventricular node ablation. The initial pacing rate after ablation should be 70 to 90 bpm [1]. This strategy does not impair left ventricular function and may even improve LVEF in selected patients [1].

We have reviewed the key updates in the diagnosis and management of atrial fibrillation. The 2024 ESC guidelines include numerous detailed tables and algorithms that outline management strategies for patients with various comorbid conditions.

CONCLUSION

The primary innovation of the 2024 ESC guidelines on atrial fibrillation management, developed in collaboration with the European Association for Cardio-Thoracic Surgery, is the adoption of the AF-CARE principles for patient management. A major update is that sex is no longer considered a risk factor for ischemic stroke or

Dronedarone is currently not registered in the Russian Federation.

systemic thromboembolism. The CHA₂DS₂-VA score is now recommended for risk stratification. The HAS-BLED score is no longer mandatory for bleeding risk assessment. Several bleeding risk scores are proposed, emphasizing that a high estimated risk should not preclude anticoagulant therapy but warrants careful evaluation and risk factor modification. Strategies and algorithms for sinus rhythm restoration and management of various AF subtypes are updated. Indications for catheter ablation, with an increased recommendation class for AF ablation are expanded. Greater emphasis on AF screening, early detection, arrhythmia prevention, comorbidity management, and risk factor modification is made.

ADDITIONAL INFORMATION

Author contribution. T.N. Novikova, writing the main part of the text, literature review, making final edits; F.I. Bitakova, S.A. Sayganov, literature review; D.A. Kunshin, L.S. Dyatchina, I.A. Dolinina, V.I. Novikov, writing the text, literature review. All authors confirm that their authorship complies with the international ICMJE criteria (all authors have made a significant contribution to the development of the concept

and preparation of the article, as well as read and approved the final version before its publication). 11

Competing interests. The authors declare that they have no conflict of interest.

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

ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Вклад авторов. Т.Н. Новикова — написание основного текста, обзор литературы, внесение окончательной правки; Ф.И. Битакова, С.А. Сайганов — обзор литературы; Д.А. Куншин, Л.С. Дятчина, И.А. Долинина, В.И. Новиков — написание текста, обзор литературы. Все авторы подтверждают, что их авторство соответствует международным критериям ICMJE (внесли существенный вклад в разработку концепции и подготовку статьи, прочли и одобрили финальную версию перед публикацией).

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

Источник финансирования. Авторы заявляют об отсутствии внешнего финансирования при написании статьи.

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DOI: https://doi.org/10.17816/cardar640825

Radiofrequency ablation of the pulmonary vein ostia in elderly patients with atrial fibrillation

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ABSTRACT

BACKGROUND: Restoration and maintenance of sinus rhythm is one of the most important aspects of managing patients with atrial fibrillation. The greatest effectiveness is achieved when this intervention is performed in young patients without comorbidities and in patients with paroxysmal atrial fibrillation. The appropriateness of performing radiofrequency ablation of the pulmonary vein ostia in elderly patients with atrial fibrillation remains a subject of debate.

AIM: to study the immediate and long-term results of catheter ablation in elderly patients with AF.

MATERIALS AND METHODS: The study group consisted of 88 patients aged 75–88 years who underwent RFA of the pulmonary vein ostia. The technique used was classical, with femoral puncture access, and irrigated ablation catheter. Data analyzed included ECG parameters, incidence of systemic thromboembolic complications, functional class of chronic heart failure according to NYHA, subjective state post-procedure, occurrence of atrial fibrillation recurrences, and the impact of baseline clinical factors on disease recurrence.

RESULTS: In 80 patients (90.9%), atrial fibrillation did not recur during their hospital stay after radiofrequency ablation of the pulmonary vein ostia. In the long term (min 1.5, max 3.1 years), a cross-sectional observational study was conducted on 37 patients. Adherence to oral anticoagulants was 97.6%. No systemic thromboembolic events were recorded among the patients available for contact. Atrial fibrillation recurrences troubled 67.6% of patients after radiofrequency ablation. The main predictors of atrial fibrillation recurrence in elderly patients were the presence of hypertension (p=0.03) and baseline left atrial enlargement (p=0.001). Despite the high recurrence rate, there was a significant reduction in the functional class of chronic heart failure following radiofrequency ablation of the pulmonary vein ostia (p=0.009).

CONCLUSIONS: Strict selection is required for performing catheter ablation in patients with atrial fibrillation older than 75 years. Significant left atrial enlargement and uncontrolled hypertension are major limitations for performing RFA of the pulmonary vein ostia in the elderly. The procedure demonstrates significant effectiveness in terms of reducing chronic heart failure functional class in patients over 75 years old, despite the high recurrence rates in the long term.

Keywords: atrial fibrillation; radiofrequency catheter ablation; surgical treatment of cardiac rhythm disorders; elderly patients.

To cite this article

Marinin VA, Sotnikov AV, Stepanova VV, Savelyeva MA, Urazovskaya IL. Radiofrequency ablation of the pulmonary vein ostia in elderly patients with atrial fibrillation. *Cardiac Arrhythmias*. 2024;4(3):15–24. DOI https://doi.org/10.17816/cardar640825

Received: 30.10.2024 **Accepted:** 17.01.2025 **Published online:** 10.03.2025



DOI: https://doi.org/10.17816/cardar640825

Радиочастотная абляция устьев легочных вен у пациентов старческого возраста с фибрилляцией предсердий

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РИПИТОННЯ

Актуальность. Восстановление и поддержание синусового ритма сердца является одним из важнейших аспектов ведения пациентов с фибрилляцией предсердий. Наибольшая эффективность достигается при выполнении данного вмешательства у некоморбидных пациентов молодого возраста и при пароксизмальной форме фибрилляции предсердий. Целесообразность выполнения радиочастотной абляции устьев легочных вен у больных с фибрилляцией предсердий старческого возраста на сегодняшний день остается предметом дискуссий.

Цель — изучить ближайшие и отдаленные результаты радиочастотной абляции устьев легочных вен у больных с фибрилляцией предсердий старческого возраста.

Материалы и методы. Исследуемая группа была сформирована из 88 пациентов в возрасте 75–88 лет, которым была выполнена радиочастотная абляция устьев легочных вен. Техника проведения классическая, с пункционным бедренным доступом. Анализировались такие данные, как показатели электрокардиограммы, наличие системных тромбоэмолических осложнений, функциональный класс хронической сердечной недостаточности по NYHA, субъективное состояние после вмешательства, наличие рецидивов фибрилляции предсердий, влияние исходных клинических факторов на рецидив заболевания.

Результаты. В 80 (90,9%) случаях после радиочастотной абляции устьев легочных вен за время нахождения в стационаре фибрилляция предсердий не рецидивировала. В отдаленные сроки (от 1,5 до 3,1 года) проведен поперечный обсервационный срез у 37 пациентов. Приверженность пероральным антикоагулянтам составила 97,6%. Системных тромбоэмболических осложнений среди доступных для контакта больных зарегистрировано не было. Рецидивы фибрилляции предсердий после радиочастотной абляции устьев легочных вен беспокоили 67,6% пациентов. Основными предикторами рецидива фибрилляции предсердий у больных старческого возраста стали гипертоническая болезнь (p=0,03) и исходная дилатация левого предсердия (p=0,001). Несмотря на большую долю рецидивов, выявлено значимое снижение функционального класса хронической сердечной недостаточности после радиочастотной абляции устьев легочных вен (p=0,009).

Заключение. Требуется строгий отбор пациентов с фибрилляцией предсердий старше 75 лет для проведения радиочастотной абляции устьев легочных вен. Выраженная дилатация левого предсердия и неконтролируемая артериальная гипертензия является значимым ограничением для выполнения радиочастотной абляции устьев легочных вен в старческом возрасте. Методика показывает значимую эффективность в плане снижения ФК ХСН у пациентов старше 75 лет, несмотря на большую частоту рецидивов в отдаленные сроки.

Ключевые слова: фибрилляция предсердий; радиочастотная катерная абляция; хирургическое лечение нарушений ритма сердца; пациенты старческого возраста.

Как цитировать

Маринин В.А., Сотников А.В., Степанова В.В., Савельева М.А., Уразовская И.Л. Радиочастотная абляция устьев легочных вен у пациентов старческого возраста с фибрилляцией предсердий // Cardiac Arrhythmias. 2024. Т. 4, № 3. С. 15-24. DOI: https://doi.org/10.17816/cardar640825

Рукопись получена: 30.10.2024 Рукопись одобрена: 17.01.2025 Опубликована online: 10.03.2025



BACKGROUND

Restoration and maintenance of sinus rhythm are key aspects of managing patients with atrial fibrillation (AF). This approach not only reduces the symptoms associated with AF but also eliminates the electrical heterogeneity of the myocardium, which otherwise leads to cardiac chamber remodeling and chronic heart failure (CHF). However, in many patients requiring sinus rhythm restoration and maintenance, this goal cannot be achieved without invasive techniques. Currently, one of the recommended methods in cases when conservative therapy proves ineffective is radiofrequency ablation (RFA) of the pulmonary vein ostia and/or other arrhythmogenic foci of the atria [1]. The radiofrequency ablation of the pulmonary vein ostia has been demonstrated to be highly effective in patients with paroxysmal AF and in patients of young and middle age [2]. The feasibility of this intervention in patients with a long history of other cardiac disorders and a high degree of cardiovascular comorbidity is still controversial. This group primarily includes elderly patients (>75 years). Changes in the normal structure and fibrosis of the atrial myocardium, resulting in cardiac chamber dilation, significantly worsen the prognosis after RFA of the pulmonary vein ostia, making the effectiveness of this technique in elderly patients a topic of ongoing debate [3, 4].

The study aimed to assess the short-term and long-term outcomes of RFA of the pulmonary vein ostia in elderly patients.

METHODS

The study group consisted of patients from the Cardiac Surgery Department specializing in the surgical treatment of complex cardiac rhythm disorders and cardiac pacing (using X-ray surgical techniques) at the Petrovsky Clinic of the North-Western State Medical University named after I.I. Mechnikov. These patients underwent surgical treatment for AF between 2014 and 2022. The study design involved a cross-sectional analysis of the target patient group. The inclusion criteria were age over 75 years, presence of symptomatic AF poorly controlled by conservative treatment, indications for RFA of the pulmonary vein ostia according to the 2020 Russian Society of Cardiology Guidelines for Atrial Fibrillation and Atrial Flutter, ongoing optimal pharmacotherapy (including anticoagulants). A total of 88 patients aged 75-88 years were included in the study. The patients meeting the inclusion criteria were consecutively enrolled in the study group; randomization was not performed. The study did not include a control group, because a comparative analysis between elderly patients and those of other age groups was deemed unnecessary due to the limited relevance of such results. The study was conducted in accordance with Good Clinical Practice (GCP) standards. It was performed in compliance

with the principles of the Declaration of Helsinki. All patients signed a written informed consent. The anticoagulant therapy was discontinued no more than 24 hours before surgery (with the last dose taken the evening before the intervention). Primary RFA of the pulmonary vein ostia was performed in 59 patients (67.0%), secondary RFA in 24 patients (27.3%), and tertiary RFA in 5 patients (5.7%).

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The clinical characteristics of the patients are presented in Table 1. The study group included 52 female patients (59.1%) and 36 male patients (40.9%). Both paroxysmal and persistent forms of AF were observed. The analysis considered the presence of stage 2 or 3 hypertension, CHF with FC I–III according to the New York Heart Association Classification (NYHA) classification, diabetes mellitus, peripheral artery atherosclerosis, chronic kidney disease, and a history of stroke.

The assessed risk of systemic thromboembolic events according to the CHA_2DS_2 -VASc score was as follows: 2 points in 5 patients (5.7%), 3 points in 21 patients (23.9%), 4 points in 36 patients (40.9%), 5 points in 19 patients (21.6%), and 6 points in 7 patients (7.9%). The risk of bleeding according to the HAS-BLED score ranged from 1 to 2 points in all patients.

According to transthoracic echocardiography (TTE) performed at the prehospital stage, the left ventricular ejection fraction (LVEF) was 54% [51.0-58.0]. The left atrial (LA) diameter was 46.1 ± 1.7 [45.57-46.70] mm, and the pulmonary artery pressure averaged 36.5 [30.7-39.2] mm Hg.

The surgical access for RFA of the pulmonary vein ostia was performed under local anesthesia using a puncture-based groin approach. After cannulation of the right femoral vein, the coronary sinus was catheterized, and a transseptal puncture was performed. A transseptal introducer, either PREFACE® (Biosense Webster Inc., USA) or Swartztm (St. Jude Medical, USA), was inserted into the left atrium (LA), followed by the introduction of a steerable non-navigational catheter (LASSO®, Biosense Webster Inc., USA) and an irrigated ablation catheter (THERMOCOOL SMARTTOUCH® SF, Biosense Webster Inc., USA). Anatomical and electrophysiological data were collected using the 3D navigation system (CARTO® 3, Biosense Webster Inc., USA). Circular antral ablation of arrhythmogenic zones at the pulmonary vein ostia was performed to achieve complete electrical isolation, with subsequent verification of conduction block using the LASSO® catheter and magnetic navigation. During the procedure, intravenous heparin sulfate was administered at 6000 to 10,000 IU, followed by neutralization with protamine sulfate at the end of the procedure. Intraoperative monitoring included simultaneous fluoroscopic data and 12-lead ECG monitoring.

The procedure was supplemented with right atrial (RA) intervention in the form of RFA of the cavotricuspid isthmus using similar surgical equipment in 17 patients with concomitant atrial flutter. Additionally, radiofrequency

modification of the atrioventricular (AV) junction was performed in 1 patient. At the end of the procedure, a pressure bandage was applied to the puncture site, and the patient was transferred to the intensive care unit for postoperative monitoring.

The statistical analysis was performed using descriptive and analytical statistical methods implemented in SPSS Statistics v. 28 software (IBM Corp., USA). The normality of distribution was assessed using the Kolmogorov–Smirnov and Lilliefors tests. Depending on the distribution pattern, the measures of central tendency were presented as the arithmetic mean \pm standard deviation ($M \pm SD$) with a 95% confidence interval (CI) for normally distributed variables, or as the median (Me) with the interquartile range (IQR) for non-normally distributed variables (in square brackets). The factor analysis was performed using Pearson chi-square (χ^2) test. The group comparisons for quantitative variables were performed using Student t test or the Mann–Whitney U test, depending on the distribution. The comparative analysis of dependent groups was conducted using the

Wilcoxon signed rank test. The statistical hypotheses were considered confirmed at p < 0.05.

RESULTS

The mean duration of surgery for AF was 128.2 ± 41.1 [114.1–141.9] minutes. By the end of the procedure, sinus rhythm was verified by ECG monitoring in 83 (94.3%) patients; intraoperative cardioversion was required to restore the sinus rhythm in 36 (40.9%) cases. Intraoperative complications occurred in 4 patients: cardiac tamponade in 2 (2.3%) and stroke in 2 (2.3%). No cases of in-hospital death were reported.

During the hospital stay, early recurrence of AF was observed in 8 (9.1%) patients. In the other 80 (90.9%) patients, AF did not recur during the hospital stay.

The main ECG parameters during the early postoperative hospital period after RFA of the pulmonary veins were within normal (Table 2). However, a trend toward an increase in the *PR* interval duration was noted, with this parameter approaching the upper limit of normal in most patients.

Table 1. Brief Clinical Characteristics of the Study Group

Category	Absolute Number	Proportion, %
Paroxysmal atrial fibrillation	65	73.9
Persistent atrial fibrillation	23	26.1
Hypertension (stage 2 or 3)	76	86.4
Post-myocardial infarction myocardial fibrosis	9	10.2
Chronic heart failure, NYHA functional class I	5	5.7
Chronic heart failure, NYHA functional class II	52	59.1
Chronic heart failure, NYHA functional class III	31	35.2
Diabetes mellitus	18	20.4
Peripheral artery atherosclerosis	7	7.9
Chronic kidney disease	26	29.5
History of stroke	10	11.4

Table 2. Electrocardiogram Results in the Early Postoperative Hospital Period After Pulmonary Vein Radiofreguency Ablation

Parameters	Me (M ± SD)	95% CI / IQR
Heart rate, bpm (<i>Me</i>)	72.0	61.0–79.0
RR interval, s $(M \pm SD)$	0.9±0.2	0.8-0.9
PQ interval, ms (Me)	175	150–200
QRS interval, ms (Me)	90	90–100
QRST interval, ms $(M \pm SD)$	398±36	385–411
Corrected QT interval, ms $(M \pm SD)$	42±44	411–442

Note. CI, confidence interval; IQR, interquartile range.

The postoperative period ranged from 2 to 4 days, after which the patients were discharged and referred for outpatient follow-up.

During the long-term follow-up period, a cross-sectional observational study was conducted, with 37 patients available for follow-up. The mean follow-up period after RFA of the pulmonary vein ostia was 2.3 years (range: 1.5-3.1 years). Clinically, patients available for long-term follow-up did not differ significantly from the initial sample. The outcome analysis was based on the data obtained during followup visits, including outpatient examination (ECG, 24-hour ECG monitoring, TTE, and coagulation profile assessment), as well as patient-reported outcomes, in accordance with the European Society of Cardiology (ESC) guidelines on the management of atrial fibrillation [5]. The data from the other patients were lost due to the inability to contact the patients who had received treatment outside their place of residence at a federal center; fatalities could not be excluded. However, the study design was cross-sectional, so 100% follow-up in the long term was not anticipated. Additionally, the target study group consisted of elderly patients whose mean age exceeded the average age at death in the Russian Federation (according to official statistics, the average age at death in 2023 was 74 years).

During the long-term follow-up, no systemic thromboembolic events were recorded among the patients available to follow-up. Over the extended period, medication adherence remained extremely high (97.6%). The primary group of medications consisted of direct oral anticoagulants (DOACs), including apixaban in 17 (45.9%) patients, rivaroxaban in 14 (37.8%) patients, and dabigatran etexilate in 3 (8.1%) patients. Additionally, 1 (2.7%) patient received warfarin, and 2 (5.4%) patients received acetylsalicylic acid (Fig. 1).

The antiarrhythmic therapy was administered to 25 (67.6%) patients, while 12 (32.4%) patients did not receive antiarrhythmic drugs. Among those receiving antiarrhythmic

therapy, class I drugs were prescribed to 2 (5.4%) patients, class II drugs to 10 (27.0%) patients, class III drugs to 8 (21.6%) patients, and class IV drugs to 5 (13.5%) patients; combination therapy was used in 3 (8.1%) cases. None of the patients received cardiac glycosides. Other medication groups included antihypertensive therapy, prescribed to 32 (86.5%) patients, including diuretics in 11 (29.7%) cases.

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According to the NYHA classification, the distribution CHF FC after RFA of the pulmonary vein ostia was as follows: class I in 8 patients (21.6%), class II in 21 patients (56.8%), and class III in 8 patients (21.6%). No patients from the study group available for follow-up in the long-term period had class IV CHF FC.

A significant improvement in CHF FC was observed in the long-term period after RFA of the pulmonary vein ostia compared with baseline values. Although the median CHF FC in both periods was 2, the IQR showed a significant difference: the baseline CHF FC at hospitalization was 2 [1.8–2.8], whereas in the long-term period, this indicator significantly decreased to 2 [1.2–2.0], p= 0.009.

The subjective assessment of patients' condition corresponded to the severity criteria of AF manifestations according to the European Heart Rhythm Association (EHRA) score. A total of 19 patients (51.3%) reported an improvement in the quality of life and exercise tolerance after the intervention, 7 patients (18.9%) reported no changes in their condition, and 11 patients (29.7%) assessed the RFA outcome as negative.

A deterioration in general condition, manifested as a decrease in exercise tolerance, was reported by 29.7% of patients. A further analysis of this patient group revealed that the unfavorable outcome in the long term after RFA of the pulmonary vein ostia was not age-dependent (p = 0.971) (see Fig. 1).

The main factor contributing to the deterioration of condition in the long term was AF recurrence. Despite the use

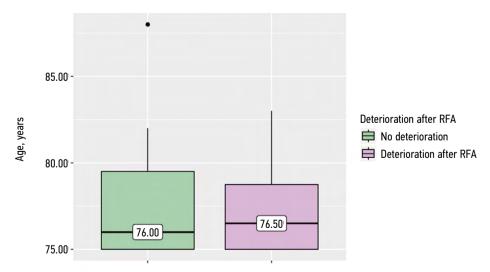


Fig. 1. Analysis of the impact of age on deterioration or condition in the long term after radiotrequency ablation of the pulmonary vein ostia (p = 0.971). The median value is shown in the center of the box plot; the box represents the interquartile range, and the "whiskers" indicate the full range of values.

of antiarrhythmic drugs, tachysystolic episodes significantly worsened quality of life and satisfaction with treatment outcomes. In patients whose condition deteriorated long after RFA of the pulmonary vein ostia, the frequency of AF recurrence was significantly higher (p = 0.007) (Fig. 2).

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AF recurrences after RFA of the pulmonary vein were observed in 67.6% of patients available for follow-up. Despite AF recurrences, not all patients rated the treatment outcome as negative. Comparing the number of patients with AF recurrence and the number of patients who negatively assessed the treatment outcome (29.7%), it can be concluded that nearly half of the patients (53.8%) did not experience a decrease in quality of life or physical exercise tolerance after RFA of the pulmonary vein ostia.

In the long term, the absence of AF recurrence was reported by only 12 (32.4%) patients. The nature of the antiarrhythmic therapy did not significantly affect the absence of AF recurrence. The significance levels for

the association between the absence of long-term AF recurrence and the class of antiarrhythmic drugs were as follows: class I, p = 1.0; class II, p = 0.445; class III, p = 1.0; class IV, p = 1.0; and no therapy, p = 0.146. The initial form of AF also had no substantial impact on the absence of recurrences (p = 0.240) (Fig. 3).

A significant association was found between long-term AF recurrence after RFA of the pulmonary vein ostia and arterial hypertension. AF recurrences were significantly more frequent in patients with hypertension (p = 0.030) (Fig. 4).

The presence of hypertension was reflected in the ECG results. The postoperative ECG data showed a tendency toward a longer PR interval in patients with hypertension: 185 ± 35 ms versus 140 ± 8 ms in patients without hypertension (p = 0.017).

When analyzing other factors influencing long-term AF recurrence after RFA of the pulmonary vein ostia, a direct association was also found between recurrence

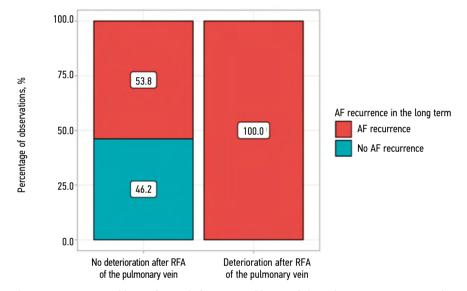


Fig. 2. Association between deterioration occurred long after radiofrequency ablation of the pulmonary vein ostia and atrial fibrillation recurrence in the study group (p = 0.007).

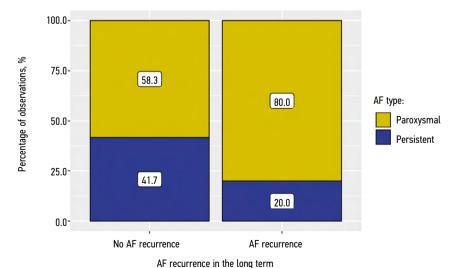


Fig. 3. Recurrence of atrial fibrillation in the study group during long-term follow-up after radiofrequency ablation of the pulmonary vein ostia, depending on the initial form of AF (p = 0.24).

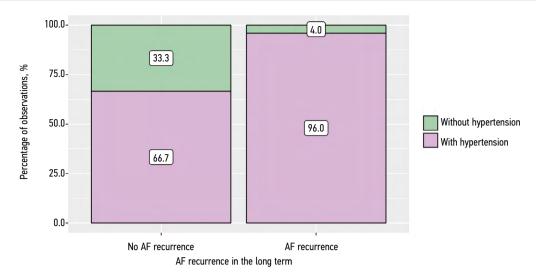


Fig. 4. Recurrence of atrial fibrillation in the study group during long-term follow-up after radiofrequency ablation of the pulmonary vein ostia, depending on the presence of hypertension (p = 0.030).

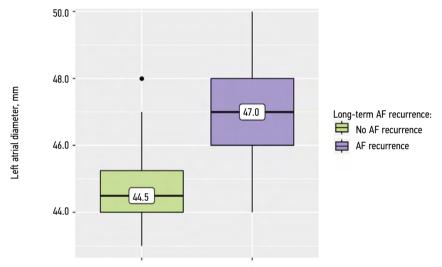


Fig. 5. Left atrial diameter according to transthoracic echocardiographic data in patients with and without atrial fibrillation recurrence (p = 0.001). The median value is shown in the center of the box plot; the box represents the interquartile range, and the "whiskers" indicate the full range of values.

and the baseline LA size. In patients with AF recurrence, the baseline LA diameter according to TTE was significantly larger: 47 [46.0-48.0] mm versus 44.5 [44.0-45.3] mm (p = 0.001) (Fig. 5).

Thus, the risk of AF recurrence primarily increased in patients with hypertension and/or LA dilation.

DISCUSSION

According to the EORP-AF registry (EURObservational Research Programme on Atrial Fibrillation), which includes 70 centers from 9 countries, 33.7% of patients with AF are aged over 75 years [6]. It has been demonstrated that AF in the elderly population significantly affects both quality of life and survival rates [4, 6]. The mortality rate among patients aged over 75 years with AF was 11.5% compared with 3.7% among patients with AF younger than 75 years. Additionally, elderly patients with AF are more likely

to develop complications within 1 year after surgery, including stroke, transient ischemic attack, and systemic thromboembolic events (13.6% in patients older than 75 years with AF compared with 4.9% in those younger than 75 years with AF).

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We observed only intraoperative complications in four patients (stroke and cardiac tamponade), which were caused by technical and clinical difficulties during surgical treatment in specific patients. The antithrombotic therapy in our study was optimally selected based on age, body weight, and comorbid conditions; however, the selected drug doses for individual patients (considering all the aforementioned factors) do not always achieve target levels to prevent systemic thromboembolic events in elderly patients. According to studies [7], in elderly patients with AF and optimal prophylaxis of systemic thromboembolic events, the incidence of ischemic stroke is 11.9%.

The key factors influencing AF recurrence were the presence of hypertension and LA size. The contribution of these two predictors to AF recurrence is not coincidental. One of the primary causes of LA dilation in patients with hypertension is chronic atrial pressure overload due to increased afterload on the LV. According to the published sources [8-10], baseline LA enlargement is one of the key predictors of recurrence after RFA of the pulmonary vein ostia. The studies have shown [11] that the risk of AF recurrence after RFA of the pulmonary vein ostia can increase by up to five times in the presence of LA dilation. Therefore, the feasibility of RFA of the pulmonary vein ostia in patients with LA dilation is questionable. It should be noted that if target blood pressure values are not achieved after RFA of the pulmonary vein ostia and hypertension persists, the risk of AF recurrence significantly increases.

Although the mean PR interval in patients after RFA of the pulmonary vein ostia remained within normal, an upward trend was observed in patients with hypertension. This finding indicated a relative slowing of impulse conduction through the atria and the atrioventricular junction. One possible reason for this could be the enlargement of both atrial chambers. An increase in the PR interval (referred to as the PR interval rather than the PQ interval in English published sources) in the general population correlates with the severity of atrial remodeling and serves as an independent predictor of future AF development [12]. Moreover, a PR interval exceeding 200 ms significantly correlates with LA size and LA volume index. There is also evidence suggesting that the recurrence rate of AF in patients with a PR interval greater than 200 ms almost doubles after RFA of the pulmonary vein ostia [13].

The high recurrence rate of AF following RFA of the pulmonary vein ostia remains an unresolved issue in modern clinical electrophysiology. The multicenter FREEZE study [10, 11] demonstrated that the recurrence rate of AF after catheter ablation averages 30%–50% within the first year. Notably, the type of energy used (radiofrequency or cryoablation) did not significantly impact recurrence rates [14]. Whereas it is generally believed that the effectiveness of repeat RFA of the pulmonary vein ostia improves with each procedure, our findings do not support this assumption. In our study, the number of RFA of the pulmonary vein ostia procedures performed in elderly patients did not influence the long-term recurrence rate.

Taking into account the high recurrence rate of AF, including asymptomatic episodes, RFA of the pulmonary vein ostia cannot be considered a superior strategy for preventing systemic thromboembolic events compared with rate control. Specifically, previous studies [15, 16] have demonstrated no significant differences in survival rates or reductions in systemic thromboembolic incidence between rhythm control and rate control strategies in AF patients over long-term follow-up. The most extensive randomized trial in this field, the CABANA Trial [17], involved 126 clinical sites across

10 countries. The patients with AF were assigned to either a rhythm control or rate control group. With anticoagulation therapy, the four-year incidence of disabling ischemic stroke was similar between the groups: 0.3% in the rhythm control group and 0.6% in the rate control group. No systemic thromboembolic events in other vascular territories were observed in either group.

During follow-up after RFA of the pulmonary vein ostia in the present study, no hospitalizations due to systemic thromboembolic events of any localization were recorded among patients available for follow-up. However, adherence to anticoagulation therapy was exceptionally high in the study cohort (97.6%). This value significantly exceeded the expected long-term adherence to anticoagulation therapy in AF patients, as reported by national and international sources [18, 19].

Despite its questionable effectiveness in preventing systemic thromboembolic events in AF patients over the long term, RFA of the pulmonary vein ostia was associated with a reduction in CHF FC in the present study. Following RFA of the pulmonary vein ostia, the mean of this parameter decreased from 2.3 ± 0.6 to 2.0 ± 0.7 (p = 0.009). The ability of RFA of the pulmonary vein ostia to improve exercise tolerance in patients with AF and concomitant CHF, despite a high recurrence rate, has been confirmed in the available publications. A detailed analysis of the CABANA Trial (2021) [20] demonstrated that in patients with AF and a baseline CHF FC greater than II, long-term survival and quality of life after RFA of the pulmonary vein ostia were significantly better than in those receiving conservative treatment.

It is important to acknowledge the limitations of our study regarding the long-term outcomes of RFA of the pulmonary vein ostia. Regrettably, long-term follow-up could not be established for 51 patients (57.9%), leaving their outcomes unknown. A major contributing factor was that most patients aged >75 years in the analysis resided in remote regions. At baseline, St. Petersburg residents accounted for only 53.4% (47 patients) of the study population. Other regions of the Russian Federation were represented as follows: 17 (19.3%) in the Republic of Karelia,8 (9.1%) in the Vologda Region, 6 (6.8%) in the Leningrad Region, 2 (2.3%) in the Novgorod Region, 2 (2.3%) in the Pskov Region, 2 (2.3%) in the Tula Region, 1 (1.1%) in the Kirov Region, 1 (1.1%) in the Rostov Region, 1 (1.1%) in the Stavropol Territory, and 1 (1.1%) person in the Tver Region. In practice, long-term follow-up for patients from remote regions is often challenging. Nevertheless, the primary cross-sectional analysis aimed to assess inhospital mortality and postoperative complications. These findings indicate the need for further research in this patient population.

CONCLUSION

Thus, considering the low incidence of postoperative complications and the absence of in-hospital mortality,

RFA of the pulmonary vein ostia appears to be a relatively safe procedure even in elderly patients with significant comorbidities. However, to minimize AF recurrences and the associated patient dissatisfaction with treatment, careful patient selection is required in this age group. The main indication for RFA of the pulmonary vein ostia in elderly patients with AF is high CHF FC or elevated EHRA scores despite optimally adjusted pharmacological therapy. A limitation to RFA of the pulmonary vein ostia in elderly patients is marked LA dilation and uncontrolled hypertension. With strict patient selection, RFA of the pulmonary vein ostia has the potential to improve CHF FC, which may positively influence long-term survival.

ADDITIONAL INFORMATION

Author's contribution. V.A. Marinin, concept and design of the study, conducting the practical part of the study, collecting data; A.V. Sotnikov, concept and design of the study, collection and processing of materials, writing the text; V.V. Stepanova, conducting the practical part of the study, collecting materials; M.A. Savelyeva, writing the text, analyzing the data obtained; I.L. Urazovskaya, analysis of the data obtained, literature review. Thereby, all authors confirm that their authorship complies with the international ICMJE criteria (all authors have made a significant contribution to the development of the concept, research, and preparation of the article, as well as read and approved the final version before its publication). Ethics approval. All patients signed an informed voluntary consent to participate in the study. The approval of the ethics committee for the study was not received due to the lack of additional interventions for patients other than those

required under the treatment plan in accordance with clinical recommendations.

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Competing interests. The authors declare that they have no conflict of interest.

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

ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Вклад авторов. В.А. Маринин — концепция и дизайн исследования, проведение практической части исследования, сбор данных; А.В. Сотников — концепция и дизайн исследования, сбор и обработка материалов, написание текста; В.В. Степанова — проведение практической части исследования, сбор материалов; М.А. Савельева — написание текста, анализ полученных данных; И.Л. Уразовская — анализ полученных данных, обзор литературы. Все авторы внесли существенный вклад в разработку концепции, проведение исследования и подготовку статьи, прочли и одобрили финальную версию перед публикацией.

Этическая экспертиза. Все пациенты подписали информированное добровольное согласие на участие в исследовании. Одобрение этического комитета на проведение исследования не получали в связи с отсутствием дополнительных вмешательств в отношении пациентов, помимо необходимых в рамках плана лечения в соответствии с клиническими рекомендациями.

Конфликт интересов. Авторы заявляют об отсутствии потенциального конфликта интересов, требующего раскрытия в данной статье.

Источник финансирования. Авторы заявляют об отсутствии внешнего финансирования при написании статьи.

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CASE REPORTS Vol. 4 (3) 2024 Cardiac Arrhythmias

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DOI: https://doi.org/10.17816/cardar643248

Arrhythmic phenotypes of cardiac laminopathies: a case series

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ABSTRACT

This article conveys clinical cases of patients with cardiac laminopathy caused by mutations in the *LMNA* gene, the early manifestations of which were supraventricular, ventricular tachyarrhythmias and conduction disorders in the absence of myocardial structural changes. Moreover, it is shown the evolution of rhythm and conduction abnormalities during the follow-up period, as well as the tendency of mutation carriers in the *LMNA* gene to develop life-threatening ventricular tachyarrhythmias and conduction disorders with a high risk of sudden cardiac death. Furthermore, herein are provided key recommendations of European and American experts regarding the concept of distinguishing laminopathies for mandatory molecular genetic testing, given that *LMNA* mutations are associated with a poor prognosis. The data obtained confirm the importance of conducting a molecular genetic study using high-throughput sequencing of genes associated with hereditary rhythm disorders, including the *LMNA* gene, in the presence of clinical manifestations such as syncope, conduction disorders (atrioventricular block, sinus node dysfunction), supraventricular and ventricular tachyarrhythmias in combination with a family history, notably in the absence of structural heart diseases. Timely molecular genetic testing may facilitate the appropriate treatment including a cardioverter-defibrillator implantation.

Keywords: laminopathy; LMNA gene; sudden cardiac death; supraventricular and ventricular tachyarrhythmias; conduction disorders.

To cite this article

Komissarova SM, Rineiska NM, Chakova NN, Dubovik AYu, Niyazova SS, Sevruk TV. Arrhythmic phenotypes of cardiac laminopathies: a case series. *Cardiac Arrhythmias*. 2024;4(3):25–34. DOI: https://doi.org/10.17816/cardar643248

Received: 20.12.2024 Accepted: 12.03.2025 Published online: 15.03.2025



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КЛИНИЧЕСКИЙ СЛУЧАЙ Tom 4, № 3, 2024 Cardiac Arrhythmias

DOI: https://doi.org/10.17816/cardar643248

Аритмические проявления кардиоламинопатии (клинические наблюдения)

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RNJATOHHA

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Представлены клинические наблюдения двух пациентов с кардиоламинопатией, обусловленной мутациями в гене *LMNA*, ранними проявлениями которой были наджелудочковые, желудочковые нарушения ритма и проводимости при отсутствии структурных изменений в сердце. Показана эволюция нарушений ритма и проводимости за период наблюдения, склонность носителей мутаций в гене *LMNA* к развитию злокачественных желудочковых тахиаритмий и нарушений проводимости с высоким риском внезапной сердечной смерти. Также приведены основные положения европейских и американских экспертов относительно концепции выделения ламиновых фенотипов для обязательного молекулярно-генетического тестирования, так как носители мутаций *LMNA* ассоциированы с плохим прогнозом. Полученные данные подтверждают важность проведения молекулярно-генетического исследования методом высокопроизводительного секвенирования генов, ассоциированных с наследственными нарушениями ритма, включая ген *LMNA*, при наличии таких клинических признаков, как синкопальные состояния, нарушения проводимости (атриовентрикулярные блокады, дисфункция синусового узла), суправентрикулярные и желудочковые тахиаритмии в сочетании с семейным анамнезом даже при отсутствии структурных нарушений миокарда, для верификации диагноза кардиоламинопатии и определения стратегии лечения. Своевременное проведение молекулярно-генетического тестирования позволяет определить оптимальную тактику лечения и необходимость профилактической имплантации кардиовертера-дефибриллятора.

Ключевые слова: ламинопатия; ген LMNA; внезапная сердечная смерть; наджелудочковые и желудочковые тахиаритмии; нарушения проводимости.

Как цитировать

Комиссарова С.М., Ринейская Н.М., Чакова Н.Н., Дубовик А.Ю., Ниязова С.С., Севрук Т.В. Аритмические проявления кардиоламинопатии (клинические наблюдения) // Cardiac Arrhythmias. 2024. Т. 4, № 3. С. 25-34. DOI: https://doi.org/10.17816/cardar643248

Рукопись получена: 20.12.2024 Рукопись одобрена: 12.03.2025 Опубликована online: 15.03.2025



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INTRODUCTION

Laminopathies constitute a group of hereditary diseases caused by mutations in the *LMNA* gene, which encodes two nuclear membrane proteins, lamin A and lamin C. These disorders exhibit marked phenotypic heterogeneity, encompassing cardiac diseases, neuromuscular disorders, and metabolic abnormalities [1]. To date, 498 *LMNA* mutations have been described, associated with >15 phenotypes [2].

The spectrum of cardiac involvement ranges from supraventricular tachycardia and/or conduction disorders to dilated cardiomyopathy (DCM) and ventricular tachyarrhythmias [3]. The clinical course of cardiac laminopathies is characterized by a high incidence of arrhythmic events, including sudden cardiac death (SCD), sustained ventricular tachycardia (VT), severe bradycardia, and high-grade atrioventricular (AV) block, even in the presence of mild left ventricular (LV) dysfunction [4]. Notably, electrical dysfunction often precedes structural heart abnormalities by several years to more than a decade, according to published data [2, 5].

In its typical form, electrical disease manifests with mild arrhythmias before or during the third decade of life. It has been reported that after the age of 30 92% of patients with *LMNA* mutations develop arrhythmias, including first-degree AV block, frequent premature ventricular contractions (PVCs), or nonsustained paroxysmal VT [6]. With age, second- or third-degree AV block typically develops and may lead to SCD [7]. Overall, 44% of patients older than 30 years eventually require pacemaker implantation due to bradyarrhythmias [6].

Supraventricular tachyarrhythmias, including atrial fibrillation (AF), atrial flutter (AFL), and focal atrial tachycardia, occur as manifestations of atrial disease. In particular, AF has been shown to progress from paroxysmal to persistent or permanent forms (45%) and is associated with a high incidence of thromboembolic complications (10% within 7 years) [2].

Ventricular arrhythmias, including cardiac arrest, VT, and ventricular fibrillation (VF), are typical manifestations of laminopathies [5, 8]. However, life-threatening arrhythmias often appear as the first clinical sign, as they are usually preceded by non-life-threatening arrhythmias or mild structural cardiac diseases[9]. The incidence SCD in cardiac laminopathies is significantly higher than that of end-stage chronic heart failure (HF), as SCD occurs at least four times more frequently than lethal outcome from HF and in 50% of cases occurs before the onset of symptomatic structural cardiac abnormalities [5]. Consequently, the only reliable method for SCD prevention is the implantation of a cardioverter-defibrillator (ICD) [6].

Although the clinical manifestations of *LMNA* mutations have been extensively described, primarily in patients with DCM phenotype, early arrhythmic manifestations, arrhythmic event progression, and the natural course of the disease remain clinically relevant.

The study aims to assess early arrhythmic manifestations in patients with cardiac laminopathies in the absence of structural cardiac abnormalities based on clinical case observations.

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CASE DESCRIPTION 1

A 23-year-old woman (Patient K.) was admitted to the cardiology department of the Republican Scientific and Practical Center of Cardiology in January 2024 with complaints of frequent palpitations accompanied by dizziness, occasional irregular heartbeats, and dyspnea during high-intensity physical exertion or while climbing more than three flights of stairs. Anamnesis morbi: the patient reported transient loss of consciousness with perioral cyanosis until the age of six, for which she was followed up by neurologists. Her syncopal episodes resolved after the age of six. Neurological examination revealed no abnormalities. There was no family history of syncope or SCD. The patient experienced arrhythmias since 2018 (Table 1). That same year, patient underwent a transesophageal electrophysiological study, which induced irregular tachycardia with a heart rate of 130-180 bpm, an ectopic P wave with varying coupling intervals, namely multifocal atrial tachycardia. In 2019, cardiac magnetic resonance imaging (MRI) revealed a left ventricular ejection fraction (LVEF) of 53%, with chamber dimensions within age-related norms. Following COVID-19 in 2020 and 2021, her condition deteriorated, with increased episodes of palpitations and irregular heartbeats. Her treatment included propafenone in combination with the β-blocker metoprolol. Before hospitalization, she had been taking ethacizine.

Upon hospital admission, the patient was in fair condition. Auscultation revealed short bursts of tachycardia with a heart rate of approximately 120 bpm. Blood pressure (BP) was 90/60 mm Hg. The initial electrocardiogram (ECG) showed rhythm and conduction disorders, including premature supraventricular contractions (PSVCs), first-degree AV block, left anterior fascicular block, and intraventricular conduction delay (Fig. 1). Transthoracic echocardiography (TTE) performed on January 12, 2024, showed LVEF of 56% and the presence of left ventricular false tendon. Considering the clinical presentation and instrumental findings, the patient underwent an endocardial electrophysiological study (EPS) and radiofreguency ablation (RFA) of the arrhythmogenic substrate, which was located in the anterior wall of the left atrium (LA) near the mitral annulus and the anterior portion of the interatrial septum at the transition to the anterior LA wall. A repeat cardiac MRI showed a slight decrease in LVEF to 51%.

Based on the patient's medical history, clinical presentation, findings from the standard 12-lead ECG and 24-hour ECG monitoring, as well as the absence of structural abnormalities on TTE and cardiac MRI, the final clinical diagnosis was multifocal atrial tachycardia with first-degree

Table 1. Evolution of rhythm and conduction disorders during 24-hour electrocardiographic monitoring

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			Identií	Identified parameters			
Examination date	Supraventricular arrhythmias	Ventricular arrhythmias	SA block	AV block, interatrial block	<i>RR</i> max, ms	Pharmacotherapy at the time of examination	Interventions
October 19, 2018	PSVCs—718 (0.3%) SVT—61 (the longest tachycardia—961 beats with HR 120/min with transient AV block)	PVCs—254 (<1%)	I	Transient first-degree AV block at night	1720	1	EPS (2018)
January 12, 2022	PSVCs—2193 (4%) SVT—258 (the longest tachycardia—86 beats with HR 121/min)	PVCs—27 (<1%)	I	Persistent first-degree AV block throughout monitoring	1960	I	I
September 21, 2023	PSVCs—2060 (3.73%) SVT—308 (the longest tachycardia—61 beats with HR 125/min)	PVCs—148 (0.15%) VT—2 (the longest tachycardia—11 beats)	I	Persistent first-degree AV block throughout monitoring	2096	ı	I
January 17, 2024	PSVCs—45 (0.1%) SVT—1 (7 beats with HR 105/min)	PVCs—172 (0.2%)	I	First-degree AV block, left anterior fascicular block	1700	Ethacizine	EPS, RFA of atrial ectopy (January 15, 2024)
March 23, 2024	PSVCs—1380 (2%) SVT—9 (the longest achycardia—7 beats with HR 105/min)	PVCs—258 (<1%) VT—1 (3 beats with HR 161/min)	Wandering atrial pacemaker within the sinoatrial node—atria	First-degree AV block, intraventricular conduction delay	1692	Metoprolol, Amiodarone	I
August 19, 2024	PSVCs—3.719 (4%) SVT—20 (the longest tachycardia—21 beats with HR 105/min)	PVCs—833 (1%) VT—4 (the longest tachycardia—6 beats with HR 126/min)	Wandering atrial pacemaker within the sinoatrial node—atria; sinus bradycardia; slow idioventricular escape rhythm	First-degree AV block, intraventricular conduction delay	1976	Metoprolol	I
September 16, 2024 (48-hour ECG monitoring)	PSVCs—1.118 (0.6%) SVT—18 (the longest tachycardia—172 beats with HR 113/min)	PVCs—1.121 (0.6%) VT—2 (the longest tachycardia—7 beats with HR 60/min)	I	First-degree AV block, left bundle branch block	2200	Metoprolol	EPS (September 17, 2024): HV Interval 86 ms. Dual-chamber pacemaker implantation (September 17, 2024)

Note: AV, atrioventricular; EPS, electrophysiological study; HR, heart rate; HV, His-ventricle interval; PSVCs, premature supraventricular complexes; PVCs, premature ventricular complexes; RFA, radiofrequency ablation; SA, sinoatrial; SVT, supraventricular tachycardia, VT, ventricular tachycardia.

AV block. The patient was discharged for outpatient follow-up with a recommendation to take bisoprolol 1.25 mg in the morning under HR and BP monitoring, with a follow-up 24-hour ECG monitoring one month after RFA.

One month after RFA, the patient reported recurrent episodes of palpitations and frequent irregular heartbeats. In March 2024, 24-hour ECG monitoring recorded supraventricular arrhythmias (2%), as well as wandering atrial pacemaker, first-degree AV block, and intraventricular conduction delay throughout the monitoring period. during ongoing therapy with metoprolol and amiodarone. In June 2024, 24-hour ECG monitoring continued to show supraventricular (<1%) and ventricular (<1%) arrhythmias, along with episodes of wandering atrial pacemaker within the sinoatrial node and atria, sinus bradycardia, and second-degree sinoatrial (SA) block type I, with a longest recorded R-R interval of 1916 ms, and first-degree AV block. In August 2024, repeat 24-hour ECG monitoring performed under ongoing metoprolol therapy revealed episodes of idioventricular rhythm (Fig. 2) and nonsustained paroxysms of ventricular tachycardia (Fig. 3). Genetic testing identified a c.241T>C (rs1553261977) nucleotide sequence variant, resulting in a tyrosine-to-histidine substitution at codon 81 of the LMNA protein sequence (p.Tyr81His). This variant has been previously reported in three patients from two unrelated families with diseases associated with LMNA gene mutations [2]. Additionally, it was observed in a patient with cardiomyopathy and skeletal muscle weakness, whose parents were not carriers of the p.Tyr81His

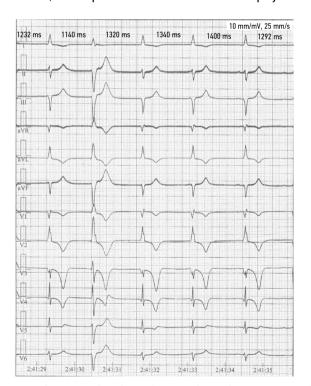


Fig. 2. A fragment of 24-hour electrocardiographic monitoring of patient K. An episode of left ventricular fascicular escape rhythm with atrioventricular dissociation

variant, suggesting a *de novo* mutation. The variant is absent from population databases, and the tyrosine residue is highly conserved. Based on the genotyping results, the diagnosis was revised to cardiac laminopathy with arrhythmia and conduction abnormalities. Direct Sanger sequencing of the patient's clinically unaffected mother did not reveal the p.Tyr81His variant in the *LMNA* gene.

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Considering the clinical presentation, laboratory and instrumental examination results, the patient was readmitted to the cardiology department in September 2024 for an EPS and further management planning. TTE revealed LVEF of 56%, hypokinesis of the basal anteroseptal and basal septal segments of the LV, and no chamber dilation. Two-dimensional strain

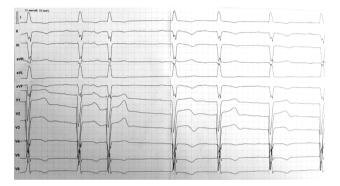


Fig. 1. Standard 12-lead electrocardiogram of patient K. at baseline. Sinus rhythm with first-degree atrioventricular block (*PR* interval, 240 ms) and left anterior fascicular block (*QRS* duration, 110 ms).

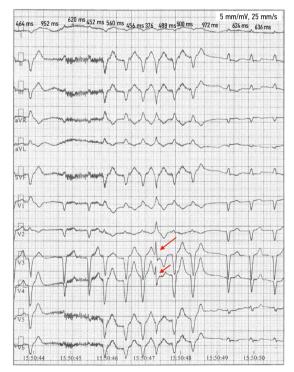


Fig. 3. A fragment of 24-hour electrocardiographic monitoring of patient K. A paroxysm of nonsustained ventricular tachycardia (fusion complexes marked with red arrows) with transformation into supraventricular tachycardia

echocardiography (2D-strain echocardiography) showed no reduction in global longitudinal strain (GLS = -20.0%) (Fig. 4). Nonetheless, further EPS demonstrated a prolonged HV interval of 86 ms (Fig. 5).

According to the 2021 European Society of Cardiology guidelines on cardiac pacing and cardiac resynchronization therapy, patients with unexplained syncope and bifascicular block are indicated for pacemaker implantation if the baseline HV interval exceeds 70 ms during incremental atrial pacing or pharmacological provocation (Class I recommendation, Level of Evidence B) [10]. Based on the EPS findings, the decision was made to implant a dual-chamber pacemaker.

After pacemaker implantation, the patient was discharged for outpatient follow-up in fair condition with a recommendation to continue metoprolol succinate 50 mg in the morning.

CASE DESCRIPTION 2

A 41-year-old woman (patient P.) was admitted to the cardiac surgery department with complaints of weakness, malaise, and anxiety. According to the patient, in 2013, at the age of 32, she experienced dizziness, and an examination revealed conduction disorders—second-degree AV block and

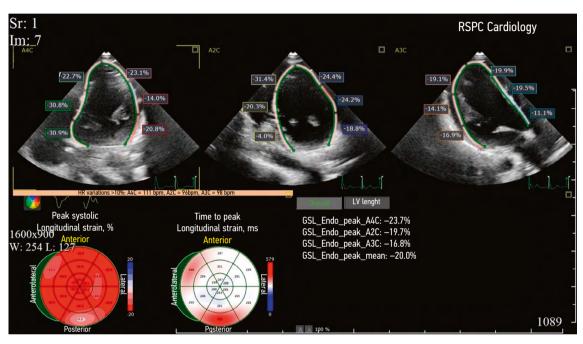


Fig. 4. Two-dimensional strain echocardiography of patient K. Left ventricular global longitudinal strain (-20.0%).

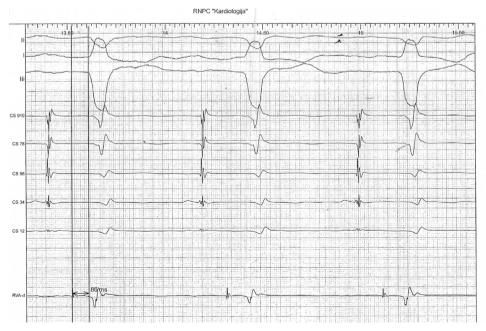


Fig. 5. Endocardial electrophysiological study of patient K. HV interval prolongation (86 ms).

second-degree SA block. That same year, a pacemaker was implanted. In 2016, pacemaker lead revision was performed due to lead displacement. In November 2021, following COVID-19, the patient experienced an episode of VT/VF, which was terminated by electrical cardioversion. TTE showed no valvular abnormalities, pacemaker leads were detected in the right heart chambers, and LVEF was 69%, indicating preserved left ventricular systolic function. ECG revealed sinus rhythm with a HR of 72 bpm, inverted *T* waves in leads *V1–V4*, and flattened *T* waves in leads *V5–V6* (Fig. 6). Coronary angiography demonstrated intact coronary arteries. An EPS was performed: during programmed stimulation

of the right ventricular apex with three extrastimuli without adrenaline (St1-St2-St3-500-240-150-240), an induced sustained VF episode occurred (Fig. 7), which was terminated by 150 J electrical cardioversion. Based on the EPS findings, the decision was made to replace the pacemaker with an ICD.

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A genetic study identified a novel nucleotide sequence variant, c.1409A > C, in exon 11 of the *LMNA* gene, resulting in a lysine-to-threonine substitution at position 470 of the protein sequence (p.Lys470Thr). This amino acid position is highly conserved among vertebrate species. *In silico* analysis predicts that this alteration causes deleterious changes to the protein. Additionally, likely pathogenic missense mutations

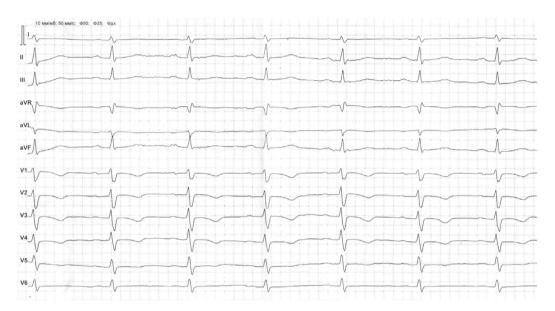


Fig. 6. Twelve-lead electrocardiogram of patient's P. showing T-wave inversion in leads V1-V4.

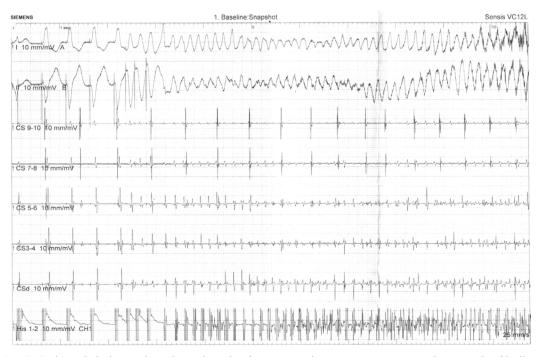


Fig. 7. Endocardial electrophysiological study of patient P. demonstrating sustained ventricular fibrillation.

have been reported in adjacent positions (p.Arg471His, p.Arg471Gly, p.Trp467Arg, etc.), further supporting the functional significance of this region. Based on the preponderance of currently available evidence, this variant

DISCUSSION

is classified as likely pathogenic.

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In these clinical cases, we have provided a detailed description of the spectrum and evolution of arrhythmic events in carriers of *LMNA* gene mutations who had no structural abnormalities detected by cardiac imaging. Notably, atrial arrhythmias and conduction disorders are frequently observed in laminopathy and may contribute to the progression of atriopathy in affected patients. Therefore, the mechanism underlying *LMNA* mutation—associated atriopathy requires further investigation. Herein, we confirmed the predisposition of *LMNA* mutation carriers to malignant ventricular tachyarrhythmias [11]. In Patient P., sustained VT with transformation into VF developed after an 8-year follow-up period, leading to the implantation of an ICD.

A study by Kumar et al. [2] analyzed the clinical features observed in lamin mutation carriers. The prevalence of clinical manifestations significantly increased from the initial assessment to the median follow-up (7 years): AV block from 46% to 57%, atrial arrhythmias from 39% to 63%, ventricular arrhythmias from 16% to 34%, and LV systolic dysfunction from 44% to 57%. ICDs were implanted in 59% of patients with LV systolic dysfunction or AV block. End-stage HF developed in 19% of patients, and the mortality rate was 13%. Among patients without systolic dysfunction at baseline, LV systolic dysfunction subsequently developed in 24% of cases, and end-stage HF occurred in 7%.

In 2022, the EHRA/HRS/APRS/LAHRS guidelines on the genetic diagnosis of cardiomyopathies and channelopathies were updated [12], incorporating a dedicated section on the diagnostic evaluation of laminopathies. European and American experts agree on the concept of identifying lamin phenotypes as an indication for mandatory molecular genetic testing, given that *LMNA* mutations are associated with poor prognosis.

In the updated 2022 guidelines on the management of patients with ventricular arrhythmias and SCD prevention, as well as the 2023 guidelines on cardiomyopathy management, SCD risk stratification was refined in the subgroup of patients with LMNA mutations [13, 14]. The association of LMNA mutations with early atrial and ventricular arrhythmias, conduction abnormalities, and a high risk of SCD was demonstrated. A multicenter study involving 269 LMNA mutation carriers identified independent risk factors for life-threatening arrhythmias, including nonsustained VT, $LVEF \le 45\%$, male sex, and non-missense mutations [9]. Another study involving 589 LMNA mutation carriers identified AV block as an

additional risk factor. Subsequently, a *risk calculator* was developed to estimate the probability of life-threatening ventricular arrhythmias 1 [4]. For primary SCD prevention, ICD placement is recommended for patients with a predicted five-year risk of \geq 10% and a cardiac phenotype (e.g., nonsustained VT, LVEF < 50%, or AV conduction delay) to prevent unnecessary ICD implantation in mutation carriers without cardiac involvement.

Thus, the findings underscore the importance of molecular genetic testing using high-throughput sequencing of genes associated with inherited arrhythmias, including *LMNA*, in patients presenting with syncope, conduction abnormalities (AV block, sinus node dysfunction), and supraventricular or ventricular tachyarrhythmias, particularly with a family history even in the absence of structural myocardial abnormalities. This approach is crucial for confirming cardiac laminopathy and guiding optimal treatment strategies.

CONCLUSION

Supraventricular and ventricular tachyarrhythmias, along with conduction abnormalities, may represent early manifestations of cardiac laminopathy in *LMNA* mutation carriers, preceding structural myocardial alterations, systolic dysfunction, and the development of a dilated phenotype. Comprehensive medical vigilance and timely genetic testing are essential for confirming the diagnosis and optimizing treatment strategies.

ADDITIONAL INFORMATION

Authors' contribution. S.M. Komissarova, concept and design of the article, writing draft, patient follow-up; N.M. Rineiska, data curation, diagnostic studies, writing draft, review and editing, literature review; N.N. Chakova, conducting and interpreting the results of genetic analysis, writing draft; A.Yu. Dubovik, writing draft, patients' curation; S.S. Niyazova, conducting and interpreting the results of the genetic analysis; T.V. Sevruk, conducting and interpreting the results of echocardiography. Thereby, all authors confirm that their authorship complies with the international ICMJE criteria (all authors have made a significant contribution to the development of the concept, research, and preparation of the article, as well as read and approved the final version before its publication).

Consent for publication. The authors have received written informed voluntary consent from the patient's legal representatives to publish personal data.

Competing interests. The authors declare that they have no conflict of interest.

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

¹ LMNA-risk VTA calculator: Risk Prediction Score for Life-Threatening Ventricular Tachyarrhythmias in Laminopathies [Internet]. Available from: https://lmna-risk-vta.fr/. Accessed March 25, 2025.

ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Вклад авторов. С.М. Комиссарова — концепция и дизайн статьи, написание текста, динамическое наблюдение за пациентами; Н.М. Ринейская — анализ полученных данных, диагностические исследования, написание текста, обзор литературы; Н.Н. Чакова — проведение и интерпретация результатов генетического анализа пациентов, написание текста; А.Ю. Дубовик — написание текста, курация пациентов; С.С. Ниязова — проведение и интерпретация результатов генетического анализа пациентов; Т.В. Севрук — проведение и интерпретация

эхокардиографии. Все авторы внесли существенный вклад в разработку концепции, проведение исследования и подготовку статьи, прочли и одобрили финальную версию перед публикацией.

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Согласие на публикацию. Авторы получили письменное согласие законных представителей пациента на публикацию медицинских данных и фотографий.

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

Источник финансирования. Авторы заявляют об отсутствии внешнего финансирования при написании статьи.

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CASE REPORTS Vol. 4 (3) 2024 Cardiac Arrhythmias

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DOI: https://doi.org/10.17816/cardar643146

Implantation of a permanent left bundle branch pacing lead in a child after tetralogy of fallot repair. A case study

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ABSTRACT

Conduction system pacing, including His bundle and left bundle branch pacing, is an increasingly utilized strategy in adult patients with bradyarrhythmias and atrioventricular conduction disorders. This technique helps prevent the development of heart failure caused by electrical and mechanical dyssynchrony associated with chronic ventricular pacing. These outcomes support the feasibility of this technique in younger pediatric patients under comparable clinical conditions. A distinct category includes children who have undergone congenital heart defect correction and require permanent cardiac pacing. These patients are at higher risk of developing pacing-induced cardiomyopathy due to non-physiologic ventricular contraction, while options for prevention and management remain limited. Biventricular pacing is technically challenging in pediatric patients, and algorithms for minimizing ventricular pacing cannot be applied in the presence of complete atrioventricular block. We report a case of left bundle branch pacing in a child with a history of surgical repair of tetralogy of Fallot and implantation of a permanent pacemaker for postoperative complete atrioventricular block.

Keywords: Tetralogy of Fallot; atrioventricular block; cardiac pacing; conduction system pacing; left bundle branch pacing.

To cite this article

Dishekov MR, Gorev MV, Talalaeva EA, Abramyan MA. Implantation of a permanent left bundle branch pacing lead in a child after tetralogy of fallot repair. A case study. *Cardiac Arrhythmias*. 2024;4(3):35–39. DOI: https://doi.org/10.17816/cardar643146

Received: 17.12.2024 Accepted: 27.02.2025 Published online: 15.03.2025



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КЛИНИЧЕСКИЙ СЛУЧАЙ Tom 4 № 3, 2024 Cardiac Arrhythmias

DOI: https://doi.org/10.17816/cardar643146

Имплантация электрода для постоянной электрокардиостимуляции левой ножки пучка Гиса ребенку после коррекции тетрады Фалло: клинический случай

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Стимуляция проводящей системы сердца (пучка Гиса и его левой ножки) у взрослых пациентов является все более распространенным методом лечения брадиаритмий и нарушений атриовентрикулярной проводимости. Эта методика позволяет предупредить развитие сердечной недостаточности, вызванной электрической и механической диссинхронией, возникающей при постоянной стимуляции желудочков. Эти данные позволяют предположить успешность применения данной технологии также у детей младшего возраста в похожих клинических обстоятельствах. Особую категорию составляют дети, перенесшие коррекцию врожденных пороков сердца и нуждающиеся в постоянной электрокардиостимуляции. Они более склонны к развитию сердечной недостаточности на фоне нефизиологичных желудочковых сокращений, и в то же время возможности профилактики и лечения стимулятор-ассоциированной кардиопатии у них ограничены: имплантация бивентрикулярной системы сопряжена с техническими трудностями, а применение алгоритмов минимизации желудочковой стимуляции невозможно из-за стойкого нарушения атриовентрикулярной проводимости. Мы представляем клинический случай имплантации желудочкового электрода в левую ножку пучка Гиса у ребенка, ранее перенесшего радикальную коррекцию тетрады Фалло и имплантацию постоянного электрокардиостимулятора по поводу постинцизионной полной атриовентрикулярной блокады.

Ключевые слова: тетрада Фалло; атриовентрикулярная блокада; электрокардиостимуляция; стимуляция проводящей системы сердца; стимуляция левой ножки пучка Гиса.

Как цитировать

Дишеков М.Р., Горев М.В., Талалаева Е.А., Абрамян М.А. Имплантация электрода для постоянной электрокардиостимуляции левой ножки пучка Гиса ребенку после коррекции тетрады Фалло: клинический случай // Cardiac Arrhythmias. 2024. Т. 4, № 3. С. 35–39. DOI: https://doi.org/10.17816/cardar643146

Рукопись получена: 17.12.2024 Рукопись одобрена: 27.02.2025 Опубликована online: 15.03.2025



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INTRODUCTION

Conduction system pacing has opened a new chapter in the use of implantable antiarrhythmic devices. In particular, implantation of a ventricular lead in the left bundle branch (LBB) area minimizes electrical dyssynchrony of the left ventricle, thereby preserving its physiological activation and contraction. This technique significantly reduces the risk of pacing-induced cardiomyopathy, demonstrating its advantages, particularly in patients with septal right ventricular pacing. In some cases, it also allows permanent cardiac pacing to be considered as an alternative to cardiac resynchronization therapy [1, 2]. The successful experience with left bundle branch pacing (LBBP) in patients older than 18 years suggests the feasibility of this technique even in younger children [3]. A specific patient category includes children who have undergone congenital heart defect (CHD) correction and require permanent cardiac pacing due to incisional atrioventricular block and other conduction disturbances in the postoperative period. The most extensive experience with ventricular lead implantation in patients with CHD has been accumulated with regard to correction of perimembranous ventricular septal defects. However, there are also sporadic reports on the use of conduction system pacing (CSP) in complex congenital defects, such as tetralogy of Fallot, double outlet right ventricle, atrioventricular canal, and others [4.5].

The aim of this study is to describe a clinical case of ventricular lead implantation in the left bundle branch (LBB)

in a child who previously underwent radical correction of tetralogy of Fallot.

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CASE DESCRIPTION

At admission to Morozovskaya Children's City Clinical Hospital in Moscow, the child was 9 years old, weighed 26 kg, and had a body surface area of 0.96 m².

At the age of 9 months, the child underwent radical correction of tetralogy of Fallot. The early postoperative period was complicated by complete atrioventricular block, requiring the implantation of a pacemaker system with an epicardial lead to the left ventricle. For 8 years, the patient was on continuous single-chamber ventricular pacing in VVIR mode, then a pacemaker replacement was carried out due to battery depletion. During routine testing, ventricular lead fracture and dysfunction were detected, prompting the recommendation to replace the epicardial system with an endocardial dual-chamber system, including ventricular lead implantation into the left bundle branch (LBB).

The preoperative electrocardiogram (ECG) showed epicardial left ventricular pacing in VVI mode with a *QRS* complex duration of 152 ms (Fig. 1*a*). According to the Echo data, left ventricular contractile function was normal prior to surgery.

Using a specialized delivery system designed for targeted lead implantation in the His bundle region (Select Site C315 His, Medtronic, USA; 2.4 mm [7Fr] diameter), a stylet-free active fixation lead (Select Secure 3830, Medtronic, USA;

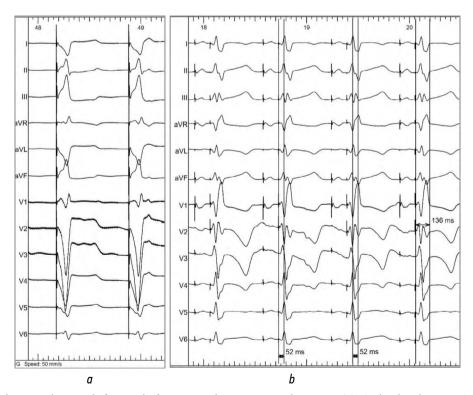
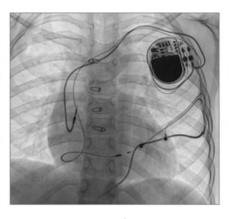


Fig. 1. Twelve-lead electrocardiogram before and after pacemaker system replacement: (a) single-chamber ventricular pacing via an epicardial ventricular lead; (b) sequential dual-chamber pacing with left bundle branch pacing. $ST-V_6$ interval, 52 ms; V_6-V_1 interval, 52 ms; QRS duration, 136 ms.

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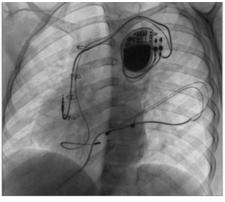


Fig. 2. Chest radiography after implantation of an endocardial dual-chamber pacemaker system with a ventricular lead in the left bundle branch: (a) right oblique view; (b) anteroposterior view; (c) left oblique view. © Dishekov et al., 2024.

59 cm long) was screwed into the interventricular septum under fluoroscopic guidance, with monitoring of electrical impedance and stimulated QRS morphology. The impedance at the final lead placement site was 923 ohm; the R-wave amplitude ranged 9.6–11.3 mV; the pacing threshold was 0.5 V with a pulse duration of 0.40 ms. The QRS complex duration in lead V_6 was 134 ms; the peak-to-peak interval (RV₁–RV₆) was 52 ms; the St–RV₆ interval was 52 ms. The atrial lead was implanted in the right atrial appendage. Upon completion of the procedure, a multi-projection assessment of lead positioning was performed (Fig. 2). The pacemaker was programmed to DDD mode with a basic pacing rate of 70 bpm. Left bundle branch pacing (LBBP) enabled a more physiological pacing mode, reducing the QRS complex duration from 152 ms to 136 ms (see Fig. 1b).

CONCLUSION

In some cases, the correction of certain congenital defects, such as tetralogy of Fallot, may require the implantation of a permanent pacemaker, making patients lifelong-dependent on permanent cardiac pacing. The lead implantation site largely determines the prognosis and the risk of complications. For example, it is now well established that right ventricular apical lead placement is strongly associated with a high risk of intraventricular and interventricular electrical and mechanical dyssynchrony, which may ultimately contribute to the development of pacing-induced cardiomyopathy. Accumulating experience with His bundle and bundle branch pacing indicates a more favorable prognosis and the achievement of more physiological conduction, contributing to an increase in conduction system pacing procedures.

ADDITIONAL INFORMATION

Authors' contribution. All the authors participated in the clinical case and the preparation of the article, read and

approved the final version before publication. M.R. Dishekov, study design and concept, text writing, pacemaker implantation; M.V. Gorev, participation in the pacemaker implantation procedure, text edit, preparation for the publication; E.A. Talalaeva, participation in the pacemaker implantation procedure, text writing, scientific consulation; M.A. Abramyan, study design and concept, text edit.

Consent for publication. The authors have received written informed voluntary consent from the patient's legal representatives to publish personal data.

Competing interests. The authors declare that they have no conflict of interest.

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

ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Вклад авторов. М.Р. Дишеков — концепция и дизайн исследования, написание текста, выполнение операции; М.В. Горев — выполнение операции, коррекция текста, подготовка к публикации; Е.А. Талалаева — выполнение операции, написание текста, научное редактировании; М.А. Абрамян — концепция исследования, научное консультирование, коррекция текста. Все авторы подтверждают, что их авторство соответствует международным критериям ICMJE (внесли существенный вклад в разработку концепции и подготовку статьи, прочли и одобрили финальную версию перед публикацией).

Согласие на публикацию. Авторы получили письменное информированное добровольное согласие законных представителей пациента на публикацию персональных данных. **Конфликт интересов.** Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Источник финансирования. Авторы заявляют об отсутствии внешнего финансирования при написании статьи.

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