Volume 14, № 50, June 2026
ISSN: 2311 — 1623 (Print)
ISSN: 2311 — 1631 (Online)
http://www.heart-vdj.com

International Heart and Vascular Disease Journal

Journal of the Cardioprogress Foundation

Antiarrhythmic drugs: efficacy, safety, and prescribing guidelines

Remote monitoring in elderly patients with chronic heart failure after pacemaker implantation

Cardiovascular risk with longterm use of proton pump inhibitors

International Heart and Vascular Disease Journal
Journal of the Cardioprogress Foundation

The *International Heart and Vascular Disease Journal* is a peer-reviewed open access publication printed quarterly. The journal features original research articles, case reports, clinical reviews, editorials, and letters to the Editor. All published articles are freely accessible from the journal's website.

The publication of articles within the journal is free of charge for authors. Guidelines for authors on submitting manuscripts are available at: www.heart-vdj.com

CONTACT DETAILS:
Cardioprogress Foundation and Editorial Office:
Room 213, Building 2, Prospect Gostinichny 6, Moscow 127106, Russia
Editorial Office tel.: (+7) 965 236 1600
Official website: http://www.heart-vdj.com

Editorial correspondence should be sent to:
Mekhman Mamedov, Editor-in-Chief,
editor.ihvdj@gmail.com
Articles for publication should be sent to:
Anna Arteyeva, Associate Editor,
submissions.ihvdj@gmail.com

Printed in Russia

The Journal is in the List of the leading scitntific journals and publications of the Supreme Examination Board (VAK)

Complete versions of all issues are published:
www.elibrary.ru, www.cyberleninka.ru

International Heart and Vascular Disease Journal

Journal of the «Cardioprogress» Foundation

Volume 14, № 50, June 2026

Contents

Editor's Welcome

Dear colleagues!

We present to your attention the next, fiftieth issue of the International Journal of Heart and Vascular Diseases, which features a leading article, original papers, and review articles.

Leading Article section opens with a review on the mechanisms of action, efficacy, safety profiles, and treatment initiation with available antiarrhythmic drugs. The presented data are intended to ensure the achievement of therapeutic goals without compromising patient safety.

Original Articles section includes three papers. The first paper determined the prevalence of hypertriglyceridemia (HTG) and assessed its relationship with markers of renal dysfunction in chronic kidney disease (CKD). The study used clinical, laboratory, and instrumental data from 562 patients with CKD of nondiabetic aetiology. In patients with CKD, HTG is more common at the stage of renal failure and is closely associated with markers of renal dysfunction. The association of HTG with cardiovascular risk factors is more pronounced in men. The second paper evaluates the relationship between morning salivary cortisol concentration and key clinical parameters in patients with cardiovascular risk factors. Elevated salivary cortisol, as a marker of chronic hypercortisolism, is associated with more pronounced dyslipidaemia (hypertriglyceridemia, abnormal lipoprotein ratio), abdominal obesity, and a higher prevalence of atherosclerotic lesions in the major arteries. The third paper is devoted to assessing the impact of remote telemetric monitoring on the course of chronic heart failure (CHF), functional status, and quality of life in patients over 60 years of age after implantation of dualchamber pacemakers (PPMs). The prospective study included 95 patients with a mean age of 72.5±7.9 years. Remote monitoring was performed using the CareLink Network remote monitoring system (Medtronic, USA). In patients over 60 with CHF, pacemaker implantation leads to a significant improvement in clinical status, functional status, and quality of life regardless of the followup method. At the same time, a significant increase in the 6minute walk test distance at one year was achieved only with the use of remote monitoring.

Review Articles section includes two papers. The first paper analyses cardiovascular risk associated with longterm use of proton pump inhibitors (PPIs). Increasing awareness among physicians and patients about the appropriate use of PPIs and knowledge of the adverse effects of longterm therapy will help optimise the use of these drugs in realworld clinical practice, especially in comorbid patients with cardiovascular pathology. The second paper presents data on the diagnosis and treatment of Fabry disease. To date, a comprehensive understanding of the aetiology, pathogenesis, and consequently the clinical manifestations of the disease has not been achieved, which leads to late diagnosis and a lack of timely pathogenetic therapy. Further research is required to identify factors involved in the early diagnosis of the disease in patients with Fabry disease.

We invite all authors to cooperate with our journal. We look forward to receiving original articles, literature reviews, discussions, opinions on current issues, as well as treatment and prevention recommendations.

Mekhman N. Mamedov
Editor-in-Chief
President of the "Cardioprogress" Foundation

International Heart and Vascular Disease Journal. Volume 14, № 50, June 2026
ISSN: 2311-1623 (Print)
ISSN: 2311-1631 (Online)
http://www.heart-vdj.com

Review of international medical news

Scientists have assessed the prognostic value of the low-density to high-density lipoprotein cholesterol ratio (LDL/HDL) for evaluating stroke risk in patients with cardio-reno-metabolic syndrome.

The analysis was conducted among 7,867 participants with cardio-reno-metabolic syndrome from the CHARLS database for the period 2011–2020. During the follow-up period, stroke developed in 501 participants, accounting for 6.4% of the sample.

The study showed that the LDL/HDL ratio was associated with an increased risk of first-ever stroke. The incidence of the disease increased with the rise in the LDL/HDL ratio, from 4.5% in the group with the lowest ratio to 7.9% among participants with the highest ratio.

The authors concluded that early detection and correction of elevated levels may improve risk stratification and enhance the effectiveness of stroke prevention.

According to the Atherosclerosis

Specialists from the University of Bristol evaluated the outcomes of surgical treatment and factors influencing mortality in patients with aortic valve endocarditis.

An analysis was conducted on data from 3,694 patients with native aortic valve endocarditis who underwent aortic valve replacement between 1996 and 2019. Participants were divided into survivor and non-survivor groups, with in-hospital mortality after surgery as the primary outcome.

The analysis showed that in-hospital mortality was 7.85% and decreased over the study period.

Thus, it was demonstrated that the urgency of surgery and the need for preoperative inotropic support are associated with an increased risk of in-hospital mortality in patients with native aortic valve endocarditis.

According to the Open Heart

Scientists have found that the use of hydroxychloroquine in patients with cutaneous forms of systemic lupus erythematosus was associated with a lower risk of cardiovascular complications and metabolic disorders.

Data from two groups of patients with discoid lupus erythematosus without other autoimmune diseases were analyzed. The first cohort included 106 patients from the Johns Hopkins Medical Center, and the second included 4,520 participants from the TriNetX database. The risk of various cardiovascular complications was assessed over a 5-year follow-up period.

The analysis showed that among patients taking hydroxychloroquine, hyperlipidemia developed significantly less frequently compared to patients without such therapy — in 23.3% of cases versus 47.8%.

According to the researchers, the drug may be considered a promising first-line therapy option in some patients with this disease.

According to the Journal of the American Academy of Dermatology

According to data from scientists in Paris, common food preservatives increase the risk of developing cardiovascular diseases and arterial hypertension.

The study involved 112,395 people with a mean age of 42.8 years. The mean follow-up period was 7.9 years.

The analysis showed that people who consumed the highest amounts of preservatives had a 29% increased likelihood of developing hypertension compared to those who ate foods with low preservative content. The risk of cardiovascular diseases under the influence of preservatives increased by 16%.

The authors conclude that both the preservatives themselves and antioxidants, which also keep food fresh by slowing oxidation, had an impact.

According to the Journal of the European Heart Journal

As part of the REGARDS cohort study, specialists assessed how a history of myocardial infarction affects subsequent cognitive decline.

Data from 20,923 people without baseline cognitive impairment enrolled in the REGARDS study from 2003 to 2007 were analyzed. The median follow-up was 10.1 years. Demographic factors, cardiovascular risk factors, and subsequent cardiovascular events were also included in the analysis.

A history of myocardial infarction was associated with faster cognitive decline over a long follow-up period. Notably, cognitive decline was observed after both clinically confirmed and silent (asymptomatic) infarctions.

According to the Journal of the Circulation

Scientists evaluated the impact of physical activity intensity on the risk of developing chronic diseases. Just a few minutes of vigorous physical activity per day substantially reduced the risk of disease and mortality. Importantly, not only the duration but also the intensity of the activity mattered.

The results indicate that a higher proportion of vigorous activity was associated with a reduced risk of major chronic diseases, including cardiovascular disease, type 2 diabetes, and dementia.

Thus, even short periods of vigorous physical activity can significantly reduce the risk of chronic diseases and mortality, and increasing the proportion of such activity in daily life improves the long-term prognosis for complications.

According to the European Heart Journal

DOI: 10.24412/2311-1623-2026-49-5-18

Antiarrhythmic drugs: efficacy, safety, and rules of use

Kanorsky S.G.[1], **Mamedov M.N.**[2]

[1] Kuban State Medical University, Ministry of Health of Russia, Krasnodar, Russia.
[2] National Medical Research Center for Therapy and Preventive Medicine, Ministry of Health of Russia, Moscow, Russia.

AUTHORS

Sergey G. Kanorsky*, PhD, MD, Professor, Head of the Department of Therapy No. 2, Kuban State Medical University, Krasnodar, Russia. ORCID: 0000-0003-3370-3506

Mekhman N. Mamedov, PhD, MD, Professor, Head of the Department of Secondary Prevention of Non-communicable Diseases, National Medical Research Center for Therapy and Preventive Medicine, Moscow, Russia. ORCID: 0000-0001-7131-8049

The progress of invasive methods for treating cardiac arrhythmias is constrained by limited access to the arrhythmogenic substrate and its complexity, procedural risks, and the high prevalence of certain arrhythmias, which makes it impossible to perform invasive interventions for all patients in need within the context of modern healthcare. The selection and administration of antiarrhythmic therapy often pose a challenging task for practicing physicians.

Objective. The aim of this review is to provide up-to-date information on the mechanisms of action, efficacy, safety profiles, and treatment initiation strategies for available antiarrhythmic drugs (AADs).

Materials and methods. A literature search focusing on the clinical use of AADs was conducted in the Russian scientific electronic library eLibrary.ru and the PubMed biomedical research database to identify articles using the keywords: "antiarrhythmic drugs", "cardiac arrhythmias", "drug therapy", "efficacy", and "safety".

Results. Currently, AADs remain the preferred means for terminating and preventing most tachyarrhythmias; they can serve as a reserve therapy and often act as a useful adjunct to catheter ablation procedures or implantable cardioverter-defibrillator implantation. The prescription of AADs is aimed at achieving the primary goal — clinical efficacy. However, the narrow therapeutic range of AADs complicates their use in practice, requiring strict adherence to administration guidelines.

Conclusion. This review is based on the results of landmark scientific studies and recent clinical guidelines for the management of cardiac arrhythmias. The information contained herein is intended to achieve therapeutic goals without compromising patient safety.

Keywords: antiarrhythmic drugs, cardiac arrhythmias, drug therapy, efficacy, safety.

Conflict of interest: none declared.

* Corresponding author. Tel. +7 (918)355-82-81. E-mail: kanorskysg@mail.ru

International Heart and Vascular Disease Journal. Volume 14, № 50, June 2026
ISSN: 2311-1623 (Print)
ISSN: 2311-1631 (Online)
http://www.heart-vdj.com

Received: 26.02.2026
Accepted: 04.05.2026

For citation: Kanorsky SG, Mamedov MN. Antiarrhythmic drugs: efficacy, safety, and rules of use. International Heart and Vascular Disease Journal. 2026;14(50): 4-15. DOI: 10.24412/2311-1623-2026-49-5-18

Introduction

Cardiac arrhythmias have a significant negative impact on the health of people worldwide. In recent decades, attempts have been made to find a radical solution to the problem of cardiac arrhythmias through invasive procedures. However, despite the success of invasive treatment with catheter ablation, issues regarding anatomical limitations for interventions, procedural risks, and arrhythmias with a complex myocardial substrate remain unresolved. Furthermore, the high prevalence of certain rhythm disorders limits the role of invasive treatments. For example, atrial fibrillation (AF), the most commonly diagnosed sustained arrhythmia, currently affects up to 7% of the adult population [1]. The need for its invasive treatment exceeds the capacity of healthcare systems in most regions. Even in countries with the most advanced medical care, currently only about 1% of patients with AF undergo catheter ablation. Moreover, according to forecasts, in the foreseeable future this figure will reach only 10% due to limited resources and the shortage of welltrained medical personnel to perform technically complex interventions [2].

For some patients, pharmacological treatment remains critically important, either because of ineffective ablation or for perioperative therapy. At least 50% of patients with AF after ablation of the arrhythmogenic substrate still require antiarrhythmic drugs (AADs). Due to the failure of the first procedure, a significant proportion of patients undergo repeat ablation, but even after that, AADs are still required in most cases [3]. Thus, in modern clinical practice, rhythm control in patients with AF often requires a combination of catheter ablation and AADs [4]. Similarly, in patients with implantable cardioverterdefibrillators (ICDs) and recurrent ventricular tachyarrhythmias (VT), AADs play a crucial preventive role. Arrhythmogenic channelopathies are generally not amenable to ablation, so they also require the use of AADs [5]. In addition, AADs are widely used in the emergency treatment of arrhythmias.

Materials and methods

A search of literature sources on the clinical use of AADs was conducted in the Russian scientific electronic library eLibrary.ru and the PubMed biomedical research database to identify articles using the keywords "antiarrhythmic drugs," "cardiac arrhythmias," "drug treatment," "efficacy," and "safety." During the screening of identified articles, preference was given to recent, highly cited Englishlanguage publications from journals with high impact factors, focusing on human studies and available in fulltext format. In addition, reference lists of suitable articles, including reviews, were examined for publications not previously identified. After excluding duplicates and articles that did not meet the inclusion criteria, 46 articles most relevant to the objectives of this literature review were selected for citation.

Results

Potential roles of antiarrhythmic drugs in clinical practice

AADs are often an appropriate and, in many cases, the only therapy needed to treat cardiac arrhythmias, including as a means of acute termination, prevention of recurrences, and longterm management of patients who respond well to pharmacological therapy and prefer it over invasive procedures.

AADs are used as rescue therapy when other primary treatments, such as ablation or ICDs, are unavailable, poorly tolerated, associated with increased risk, contraindicated, or ineffective for preventing or terminating arrhythmic episodes.

AADs serve as a useful adjunct to other treatments, such as catheter ablation or ICDs, during waiting periods for procedures, in the perioperative phase, and subsequently, enhancing overall treatment efficacy.

Mechanisms of action of antiarrhythmic drugs

AADs are pharmacological agents designed to prevent or treat rhythm disorders by modulating the electri-

cal activity of the heart. Cardiac arrhythmias mainly arise through three key mechanisms: abnormal automaticity, triggered focal activity caused by early or delayed after depolarisations, and reentry. The latter mechanism is recognised as the most common and requires the existence of the following main factors for its manifestation. First, a trigger is needed to initiate reentry, which can be an ectopic impulse originating from some area of the heart. Second, a reentrant circuit is required, which is a pathway along which the electrical impulse circulates in cardiac tissue, maintaining the abnormal rhythm. This is facilitated by shortened refractoriness, slowed conduction (or a combination of both), and unidirectional block. In addition, sympathetic and parasympathetic influences on the electrical properties of the heart can either increase or decrease the likelihood of arrhythmia occurrence. These must be considered when selecting AADs in specific situations [6].

AADs exert their therapeutic effects by modulating the electrophysiological determinants of automaticity, triggered activity, and reentry. Class I AADs block sodium channels in cardiomyocyte membranes, reducing myocardial excitability and decreasing the likelihood of ectopic activity [7]. They may also prolong the effective refractory period (ERP) by delaying cardiomyocyte recovery after repolarisation. Some Class I AADs additionally prolong ERP by inhibiting the rapid component of the delayed rectifier potassium current (IKr) and other repolarising currents, leading to an increase in action potential duration. Such inhibition, which results in QT interval prolongation, is the main mechanism of action of Class III AADs [7]. Prolongation of ERP reduces the probability that trigger events will lead to the development of excitable tissue (arrhythmogenic substrate) and the occurrence of arrhythmia. This explains the role of AADs in preventing recurrences of supraventricular and ventricular arrhythmias. Class III AADs act primarily by inhibiting IKr, leading to increased action potential duration. As a result, ERP is prolonged, which prevents the stability of reentry and reduces the likelihood of sustained arrhythmias, justifying the use of Class I and III AADs for pharmacological cardioversion.

Class II AADs exert numerous indirect electrophysiological effects by reducing ßadrenoceptordependent phosphorylation of numerous ion channels, proteins involved in Ca^{2+} transport, and myofilament proteins. The resulting decrease in ryanodine receptor 2 activity, together with reduced Ltype calcium current, reduces the probability of early and delayed after depolarisations and, consequently, the likelihood of ectopic (triggered) activity [8]. Inhibition of β–adrenoceptormediated regulation of hyperpolarisationactivated and Ltype calcium channels reduces automaticity in sinoatrial node cells, justifying the use of Class II AADs for the treatment of sinus tachycardia [8]. Direct inhibition of Ltype calcium channels with Class IV AADs, or indirectly with Class II AADs, slows atrioventricular (AV) conduction, providing rate control during atrial arrhythmias. Thus, the main mechanisms of action of AADs are suppression of ectopic (triggered) activity (Class I and II), reduction of reentry probability (Class I and III), and modulation of impulse generation and conduction in the sinus and AV nodes (Class II and IV).

Importance of considering pharmacokinetics and genetic polymorphism in antiarrhythmic therapy

Most AADs have a narrow therapeutic range, which underscores the critical role of considering their pharmacokinetics in optimizing treatment outcomes. The pharmacokinetics of AADs, including aspects of intestinal absorption, firstpass hepatic metabolism, tissue distribution, and renal or hepatic elimination, are crucial for therapeutic efficacy and safety. Physicians must consider these factors, along with individual patient characteristics, to appropriately select antiarrhythmic therapy and reduce the likelihood of adverse treatment outcomes [9].

Genetic polymorphism can significantly affect drug responses, metabolism, and the risk of adverse effects [10]. The efficacy and safety of AADs vary considerably among individual patients due to genetic differences affecting their metabolism, transport, and pharmacodynamics. Genetically determined activity of cytochrome P450 isoenzymes CYP2D6 and CYP3A4 influences the biotransformation of AADs, especially drugs such as flecainide and propafenone, affecting blood drug concentrations and toxicity risk. Ion channel genes (e.g., SCN5A, KCNH2) affect AAD binding and may exert proarrhythmic effects; drug transporter genes (e.g., ABCB1, encoding Pglycoprotein) alter AAD absorption and distribution. Pharmacodynamic gene variants (e.g., ADRB1, CACNA1C) determine the body's response to AADs, which can significantly affect treatment efficacy. Certain genetic mutations,

such as those associated with long QT syndrome, increase the risk of druginduced arrhythmias such as polymorphic VT (torsades de pointes).

Classification of antiarrhythmic drugs

In the early 1970s, the thenknown AADs were grouped by Vaughan Williams and Singh into three classes based on their functional and electrophysiological effects: Class I drugs reduce myocardial excitability, Class II drugs (β-blockers) exert sympatholytic effects, and Class III drugs increase the duration of repolarisation [11]. The discovery of the antiarrhythmic potential of the calcium channel blocker verapamil led to the addition of Class IV AADs. Furthermore, the differential effects of individual Class I AADs on repolarisation duration, largely due to different binding and dissociation kinetics in the sodium channel, led to further subdivision into Classes Ia, Ib, and Ic. The practicality of this classification lies in the clinical significance of the pharmacological properties on which it is based, giving rise to electrophysiological effects, indications, and adverse effects characteristic of each AAD group [12]. However, subsequent studies showed that virtually all AADs act on multiple targets in cardiomyocytes, resulting in complex electrophysiological effects that are not identical in different clinical situations and are difficult to reflect in the Vaughan Williams classification [12]. Amiodarone is an example of an AAD with pronounced inhibitory effects on a number of ion channels; although traditionally classified as a Class III AAD, it affects sodium, potassium, and calcium channels, and also blocks α and ßadrenoceptors, thereby exhibiting properties of all four classes of the Vaughan Williams classification [13]. In addition, other substances with antiarrhythmic activity that do not fit into the Vaughan Williams classification have been identified, including magnesium sulfate for the treatment of torsades de pointes and the selective inhibitor of the sinus node If current, ivabradine, originally developed to reduce heart rate (HR) in patients with coronary heart disease (CHD), but also effective in treating inappropriate sinus tachycardia [14].

The limitations of the traditional Vaughan Williams classification have led to numerous attempts to refine the classification of AADs. In the early 1990s, the "Sicilian Gambit" was proposed to integrate the multiple mechanisms of action of AADs with their clinical effects [15]. However, the Sicilian Gambit did not replace the Vaughan Williams classification in everyday clinical practice. Subsequently, several extensions to the Vaughan Williams classification were proposed to cover emerging AADs and various compounds still in development and investigation. The latest and most extensive of these is the 2018 Oxford classification of AADs [16]. This classification expands Class I with a subclass Id, subdivides Classes II and III, expands Vaughan Williams Class IV, and adds Classes 0, V, VI, and VII. Meanwhile, most AADs used in practice belong to several subclasses due to their simultaneous blocking effects on different types of ion channels and on some elements of the new classes or subclasses. Table 1 presents a simplified Oxford classification of AADs, focusing on agents available in the Russian Federation.

The Oxford classification also includes other classes deliberately not presented in Table 1: IIb (isoprena-

Table 1. **Classification of Antiarrhythmic Drugs**

Class	Subclass	Mechanism of Action	Drugs
0		**Inhibition of If channels**	**Ivabradin**
Sodium channel blockers			
I	Ia	Openstate blockade (intermediate kinetics)	Procainamide
	Ib	Inactivatedstate blockade (fast kinetics)	Lidocaine
	Ic	Open/inactivatedstate blockade (slow kinetics)	Flecainide, propafenone
	Id	Late sodium current blockade	Ranolazine
Inhibitors of the autonomic nervous system			
II	IIa	β-Adrenoceptor antagonism	β_1-selective blockers: atenolol, bisoprolol, metoprolol; β_1- and β_2-blockers: propranolol, nadolol; β_1-, β_2- and α_1-blockers: carvedilol
Potassium channel blockers			
III	IIIa	Nonselective potassium channel blockers	Amiodarone, sotalol
Calcium channel blockers			
IV	IVa	Selective calcium channel blockers	Verapamil, diltiazem

line), IIc (atropine), IIIb (nicorandil), as well as classes IIIc, IVb, V, and VI, for which there are no AADs yet approved for clinical use. Class VII includes treatments for underlying cardiovascular pathology (angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, sacubitril/valsartan, mineralocorticoid receptor antagonists, sodiumglucose cotransporter 2 inhibitors, statins) [16].

Widely Used Antiarrhythmic Drugs Available in the Russian Federation

Class 0

Ivabradine

Ivabradine is a selective inhibitor of the If current, which carries a mixed Na^+/K^+ current and plays a key role in spontaneous diastolic depolarisation of the sinus node. By directly affecting this current, ivabradine reduces the rate of spontaneous depolarisation in the sinus node, thereby slowing the heart rate without significantly affecting myocardial contractility or AV conduction. Ivabradine may be used to reduce HR and symptoms in patients with inappropriate sinus tachycardia. However, ivabradine is not recommended for patients with paroxysmal AF, as it can provoke episodes of this arrhythmia [17].

Class Ia

Procainamide

Procainamide is a Class Ia AAD that inhibits sodium channels in cardiomyocyte membranes with high affinity for the open state and intermediate dissociation kinetics, and also blocks IKr. Collectively, these effects reduce excitability, prolong ERP and action potential duration, increasing refractoriness after repolarisation, and slow conduction. The halflife of procainamide is 34 hours. The drug is eliminated 50% by hepatic metabolism and 50% by renal excretion of unchanged drug. Procainamide is used for emergency cardioversion of monomorphic VT provided haemodynamics are stable. It is also used in patients with accessory AV connections and AF with preexcitation, slowing conduction through the accessory pathway and reducing the ventricular rate [2].

Class Ib

Lidocaine

Lidocaine is a Class Ib AAD that inhibits inactivated sodium channels with fast dissociation kinetics. Lidocaine reduces automaticity and triggered activity by decreasing the slope of phase 4 of the action potential and reducing ventricular myocardial excitability. The action potential duration under lidocaine is either unchanged or shortened. However, ERP may be prolonged due to increased postrepolarisation refractoriness resulting from sodium channel inhibition. After intravenous bolus administration, plasma lidocaine concentrations decline rapidly (halflife about 8 minutes) due to rapid distribution from plasma to peripheral tissues. Thereafter, the drug is eliminated by hepatic metabolism mediated by CYP3A4, with a halflife of about 2 hours. Mortality in myocardial infarction (MI) patients receiving lidocaine was higher, possibly due to a higher incidence of asystole and bradyarrhythmias, leading to abandonment of the previously widespread use of this AAD in such situations [2].

Class Ic

Flecainide and Propafenone

Flecainide and propafenone cause potent usedependent sodium channel blockade, reduce myocardial excitability, and slow conduction in rapidly responding cardiac tissues, exerting their greatest effects on the ventricles and the HisPurkinje system. They suppress ectopic automaticity, shorten the excitation period in Purkinje fibres, but prolong it in ventricular myocardium, and increase ventricular refractoriness by prolonging sodium channel reactivation. Flecainide and propafenone increase atrial action potential duration in a ratedependent manner, which may facilitate conversion of AF to sinus rhythm. In orthodromic and antidromic AV reentrant tachycardias, flecainide and propafenone slow conduction and increase antegrade and, especially, retrograde refractoriness in accessory pathways in a ratedependent manner. Flecainide also shortens the QT interval in patients with long QT syndrome type 3 and reduces arrhythmogenic Ca^{2+} release from the sarcoplasmic reticulum in patients with catecholaminergic polymorphic VT through blockade of ryanodine receptors in the myocardium [18]. Propafenone may serve as an alternative to flecainide in catecholaminergic polymorphic VT and exhibits moderate β-blocking activity at doses > 450 mg/day. Flecainide and propafenone have minimal haemodynamic effects in patients with normal left ventricular ejection fraction (LVEF) but reduce it in patients with LV dysfunction and heart failure (HF).

Flecainide and propafenone are recommended for cardioversion of AF to sinus rhythm and for longterm maintenance [19, 20], as well as to enhance the efficacy of direct current cardioversion and reduce the risk of early AF recurrence. In selected patients with significant symptoms and infrequent paroxysmal AF episodes, a single oral loading dose of flecainide or propafenone (the "pillinthepocket" approach) may be used to restore sinus rhythm, provided its safety has been previously established in hospital and anticoagulation guidelines are followed [21].

Intravenous flecainide or propafenone can terminate supraventricular tachycardias, including focal atrial tachycardia, AF with ventricular preexcitation, and AV nodal reentrant tachycardia, while oral formulations of these AADs prevent recurrences of these arrhythmias [22].

Flecainide and propafenone may be used for prevention and treatment of lifethreatening sustained VT episodes refractory to antiadrenergic drugs or ablation, or when these are not possible or undesirable. Combination therapy of flecainide/propafenone with amiodarone may be used in patients with frequent VT recurrences who have an ICD [23].

Flecainide/propafenone can cause monomorphic VT, have been associated with HF, cardiac arrest, and increased mortality in patients with prior MI and LV dysfunction [24, 25]. Therefore, their use in patients with CHD or stable angina pectoris should be avoided. There is controversy regarding the safety of flecainide in patients with stable angina without prior MI or ventricular dysfunction [26]. Prophylactic use of flecainide and propafenone is potentially dangerous in patients with congenital heart disease [27]. Flecainide and propafenone increase QRS duration, and if it widens by > 25% from baseline, dose reduction or discontinuation is recommended. These AADs are not recommended in patients with baseline QRS >120 ms due to risk of excessive conduction delay, especially in patients with left bundle branch block or bifascicular block.

Information on Russian Class Ic AADs (diethylaminopropionylethoxycarbonylaminophenothiazine, lappaconitine hydrobromide) is detailed in a separate review article [28].

Class Id
Ranolazine

Ranolazine is an antianginal agent that selectively inhibits sodium channels and IKr, prolonging atrial and, to a lesser extent, ventricular refractory periods [29]. Ranolazine does not slow intracardiac conduction, nor does it affect HR, myocardial contractility, or blood pressure. Offlabel use of ranolazine reduced the incidence of AF after cardiac surgery and after electrical cardioversion, and in patients with stable CHD was associated with prevention of arrhythmias and reduced mortality [30]. Combination of ranolazine and amiodarone may be effective in treating AF and VT refractory to other therapies. However, ranolazine requires careful monitoring due to the risk of QT interval prolongation, including from potential drug interactions.

Class IIa
β-Adrenoceptor blockers

Chronic autonomic dysfunction contributes to cardiac remodelling, including hypertrophy, apoptosis, and myocardial fibrosis. It also promotes the progression of cardiovascular diseases, indirectly creating an arrhythmogenic substrate in the heart. Moreover, acutely occurring autonomic imbalance is a wellrecognised trigger for cardiac rhythm disorders [8, 31]. In this context, the role of β-blockers in the treatment of cardiac arrhythmias is clear. Generally, β-blockers are divided into three generations: firstgeneration β-blockers (e.g., propranolol) have similar affinity for β1- and β2-adrenoceptors; secondgeneration β-blockers (e.g., atenolol, metoprolol, bisoprolol) have higher affinity for β1-adrenoceptors; thirdgeneration β-blockers possess additional α-blocking (e.g., carvedilol) or β3-stimulating (nebivolol) properties [8]. Most proarrhythmic effects of sympathetic stimulation are linked to β1-adrenoceptors. All β-blockers suppress sinus node automaticity (negative chronotropic effect), inhibit AV conduction (negative dromotropic effect), and reduce electrophysiological heterogeneity caused by heterogeneous autonomic innervation. With longterm use, they may help prevent proarrhythmic remodelling by reducing myocardial energy consumption and attenuating oxidative stress, partly due to their negative inotropic and chronotropic effects.

Owing to their negative dromotropic effect and rapid onset, β-blockers are firstline agents for ventricular rate control in AF [32]. In addition, β-blockers suppress ventricular ectopy, reduce the likelihood of VT, appropriate and inappropriate ICD shocks, and the risk of sudden cardiac death. Overall, they reduce

morbidity and mortality in a broad range of patients, including those with acute coronary syndromes, HF with reduced ejection fraction, long QT syndrome, and catecholaminergic polymorphic VT [5]. The prognostic benefit of β-blockers in patients with HF and sinus rhythm does not extend to similar patients with AF [33]. Perioperative β-blocker therapy is commonly used to prevent AF after cardiac surgery, but is not indicated for patients undergoing noncardiac surgery [32]. If shortacting, hepatically metabolized β-blockers are ineffective, switching to renally excreted β-blockers such as nadolol may be a more effective alternative.

Class IIIa

Amiodarone

Amiodarone inhibits a broad spectrum of ion channels and receptors, including IKr, sodium and calcium channels, as well as α and ßadrenoceptors, possessing properties of all four originally proposed AAD classes [34]. As a result, it increases the duration of repolarisation (mainly through IKr inhibition) and slows conduction velocity by blocking sodium channels. Intravenous amiodarone predominantly slows ventricular conduction, causes less repolarisation prolongation, has a minor effect on HR, and exerts a more pronounced antiadrenergic effect [35]. Amiodarone has a delayed onset of action (antiarrhythmic effect stabilizes after 10 weeks of therapy) and a very long halflife (30100 days). To accelerate onset, intravenous administration and high oral loading doses are used. The initial dose may be 600 mg daily for four weeks, followed by a maintenance dose usually 100200 mg daily. Elimination is mainly via the liver and biliary tract, with almost no renal excretion [36].

Amiodarone is considered the most effective AAD currently available. Its efficacy and relatively low proarrhythmic risk are likely due to complex interactions between multiple molecular targets, leading, for example, to increased repolarisation duration without increasing repolarisation dispersion or the risk of early after depolarisations [37]. Amiodarone is one of the few AADs approved for use in patients with HF; it is used to suppress ventricular arrhythmias, to prevent VT recurrences terminated by appropriate ICD shocks, and is a firstline drug for the treatment of ventricular fibrillation [36]. Amiodarone is widely used for cardioversion of AF and subsequent longterm maintenance of sinus rhythm, being more effective than other AADs (sinus rhythm maintained at 1 year in >⅔ of patients) [32]. Amiodarone is also used for the prevention and treatment of perioperative AF in cardiac surgery [32]. The negative dromotropic effect of amiodarone may be useful for rate control in addition to β-blockers and digoxin in patients with AF, including in acute situations with haemodynamic instability [32].

Compared with other Class III AADs, amiodarone has a relatively low proarrhythmic risk, with an incidence of druginduced torsades de pointes of <1% despite QT prolongation. Therefore, amiodarone therapy may be safely continued in patients with QTc prolongation up to 550 ms, provided there are no additional risk factors such as bradycardia, electrolyte imbalance, or concomitant use of other QTprolonging drugs. At the same time, amiodarone use is limited by its potentially serious extracardiac toxicity [38]. Despite significant toxicity, amiodarone remains the most commonly prescribed AAD. In a US insurance database, it accounted for about half of all AAD prescriptions [39]. This is likely due to the high prevalence of CHD and HF in patients with supraventricular and ventricular arrhythmias; in these settings, many other AADs are contraindicated because of their increased proarrhythmic potential.

Sotalol

Sotalol is a racemic mixture of two isomers: D and Lsotalol. Lsotalol is a nonselective β-blocker with minor Class III AAD effects, while Dsotalol primarily blocks IKr. At low doses (e.g., ⩽160 mg/day), racemic sotalol mainly exerts β-blocking (Class II) effects. At doses >160 mg/day, with increasing dose, D,Lsotalol provides both ßblocking and increasing Class III antiarrhythmic effects. Sotalol slows heart rate, prolongs ERP (QT interval), and increases refractoriness throughout the heart, especially at lower HR. In the AV node, it slows conduction and prolongs the refractory period, but does not affect conduction velocity in fastresponse tissues. In patients with baseline reduced LVEF, sotalol may reduce cardiac output and precipitate HF [40].

Sotalol is less effective than amiodarone in maintaining sinus rhythm after cardioversion of AF/atrial flutter (AFL) in patients with normal left ventricular function, stable CHD, or valvular heart disease. However, it may enhance the efficacy of direct current cardioversion [41, 42]. A dose of 80 mg twice daily

may be sufficient for AF prevention, but higher doses may be needed if recurrences occur. Sotalol reduces ventricular rate during AF, but is ineffective for cardioversion of AF [32]. In patients with ICDs and ischaemic or nonischaemic VT recurring despite β-blockers, sotalol reduced the frequency of recurrent sustained VT/ventricular fibrillation, but did not improve survival [43]. After MI, longterm Dsotalol therapy significantly reduced the risk of reinfarction but not sudden cardiac death [44]. Sotalol may be used in idiopathic right ventricular outflow tract VT with severe symptoms or haemodynamic compromise. It may also be used in patients with long QT syndrome when ICDs are contraindicated or refused, or with a family history of sudden cardiac death [41]. Sotalol prolongs QT interval and dosedependently increases the risk of torsades de pointes from 0.3 to 2%, especially with renal impairment and HF [40, 41]. Sotalol is not recommended for patients with less severe arrhythmias (ventricular ectopy, nonsustained VT) even if symptomatic, and may be used for longterm therapy only with careful monitoring of QT interval, potassium levels, and creatinine clearance [5].

Class IVa

Verapamil and diltiazem

Verapamil and diltiazem block cardiac calcium channels, reduce HR and cardiac contractility, slow conduction and prolong refractoriness in the AV node, suppress abnormal automaticity in depolarised cells, and inhibit triggered activity caused by early after depolarisations [45]. They do not affect excitability, conduction velocity, or refractoriness in atrial, ventricular, or His-Purkinje myocardium. Verapamil and diltiazem should be used with caution in patients with LV dysfunction or those taking β-blockers, as HR and cardiac contractility may decrease sharply.

Owing to their AV nodedepressant effects, diltiazem and verapamil are recommended for ventricular rate control in patients with AF/AFL without ventricular preexcitation. They may be used alone or in combination with digoxin [32].

Verapamil and diltiazem are recommended for rate control in haemodynamically stable patients with supraventricular tachycardias such as focal or multifocal atrial tachycardia, inappropriate sinus tachycardia, AFL, macroreentrant atrial tachycardias, AV nodal reentrant tachycardia, and AV reentrant tachycardias without preexcitation [22].

Verapamil is recommended for idiopathic fascicular left ventricular tachycardia, in patients with symptomatic papillary muscle tachycardia, and for mitral and tricuspid annular VT [5].

Verapamil and diltiazem are contraindicated in patients with hypotension or HF with reduced LVEF, haemodynamic instability, and also in AF with ventricular preexcitation, as they may accelerate the ventricular response. Verapamil and diltiazem may cause marked haemodynamic deterioration in patients with widecomplex tachycardia of unknown origin [2].

Verapamil, compared with diltiazem, exerts greater negative inotropic and chronotropic effects, making it more effective in AF and supraventricular tachycardias; it more often causes bradycardia, worsens HF, and leads to constipation due to effects on gastrointestinal smooth muscle, and may reduce bronchospasm. Diltiazem is better tolerated and less constipating, but more often causes pedal oedema than verapamil. It is preferred in patients requiring milder heart rate or blood pressure control.

Prescribing Guidelines for Antiarrhythmic Drugs

Prescribing AADs requires thoughtful, safetyoriented actions to achieve optimal outcomes with minimal risks. This implies responsible consideration of underlying and comorbid conditions, careful monitoring, and patient education.

Treatment of the underlying disease – CHD – involves lipidlowering therapy, adequate ßblockade, myocardial revascularization when indicated, and elimination of arrhythmiaprecipitating factors such as electrolyte imbalance. Patients with HF are recommended therapy according to phenotype: with reduced ejection fraction, β-blockers, mineralocorticoid receptor antagonists, angiotensinconverting enzyme inhibitors or sacubitril/valsartan, and sodiumglucose cotransporter 2 inhibitors (dapagliflozin, empagliflozin) are prescribed; the latter play a central role in preserved ejection fraction [46].

Baseline ECG, echocardiography, assessment of renal and hepatic function, and complete blood count and biochemical tests (lipid profile, glucose, electrolytes) are recommended. When prescribing amiodarone, baseline thyroid function tests, chest X-ray, pulmonary function tests (with diffusing capacity assessment), and slitlamp ophthalmoscopy should be performed. Patients starting Class Ic AADs

Table 2. **Recommended Investigations at Initial Assessment and During Followup of Patients Receiving AADs [2]**

Investigation	Parameter	Frequency of Assessment	Toxicity Assessment
AADs other than amiodarone			
ECG	Heart rhythm, PR interval, QTc interval, QRS complex	Baseline and soon after initiation or dose adjustment (1–2 days for Class Ia AADs, sotalol) and periodically (e.g., every 6 months)	QT prolongation (Class Ia and III); QRS widening (Class Ic); Proarrhythmia (e.g., AFL with Class Ic); Bradycardia / bundle branch block / AV block
Echocardiography	Ventricular function	Baseline and if change is suspected	Systolic dysfunction (contraindication for Class Ic and IV)
Blood tests and serum electrolytes	GFR, serum K^+, Mg^{2+}	Baseline and periodically (e.g., every 6 months)	Reduced drug elimination; risk of arrhythmia
Liver function	ALT, AST, total bilirubin	Baseline and periodically (e.g., every 6 months)	Reduced drug elimination
Exercise test	QRS complex at peak exercise, myocardial ischaemia	Consider during Class Ic therapy	QRS widening on exercise
Amiodarone			
ECG	Heart rhythm, PR interval, QTc, QRS	Baseline, after full loading (1–3 months), annually	QT prolongation, proarrhythmia (e.g., in WPW syndrome), bradycardia or AV block
Echocardiography	Ventricular function	Baseline and if change is suspected	Systolic dysfunction
Serum electrolytes	K+, Mg^{2+}	Baseline and every 6 months	Risk of arrhythmia
Liver function	ALT, AST, total bilirubin	Baseline and every 6 months	Hepatotoxicity
Thyroid function	TSH, free T_4, free T_3	Baseline and every 6 months	Hypothyroidism or hyperthyroidism
Pulmonary function	Chest Xray and pulmonary function tests (diffusing capacity)	Baseline and every	Interstitial lung disease
Ophthalmic examination	Slitlamp corneal examination and ophthalmoscopy	Baseline and every	Corneal microdeposits and, rarely, optic neuropathy

may undergo an exercise test to assess QRS widening during exertion or detect subclinical myocardial ischaemia (Table 2).

When prescribing AADs, especially intravenously, it is essential to monitor blood pressure regularly, as these drugs may cause vasodilation and hypotension. Careful control of infusion rate is recommended to ensure adequate peak plasma concentration and avoid hypotension. The physician should remain with the patient during administration.

ECG parameters for monitoring/ observation during AAD infusion [2]

- Atrial rate, atrial cycle length (in AFL)
- Bradycardia
- Enhanced AV conduction, 1:1 AV conduction
- Unexpected AV block (Class Ic and III AADs)
- Termination of AF or AFL
- Signs of sinus node dysfunction upon termination of AF/AFL
- QRS widening and aberrant conduction (Class Ic AADs)
- QT prolongation (Class Ia and III AADs)
- Brugada pattern on ECG in right precordial leads (Class I AADs)
- Torsades de pointes and other ventricular arrhythmias.

Outpatient initiation of therapy is more convenient but requires appropriate monitoring using tools such as smartwatches, transtelephonic devices, or other patientactivated ECG recording methods. Any abnormalities detected on wearable electronic devices should prompt a confirmatory 12-lead ECG. The choice between inpatient and outpatient initiation is primarily based on safety considerations (Table 3).

In women and patients over 65 years of age, sotalol should be initiated on an outpatient basis only under close supervision and in the absence of other risk factors. Patients should be informed of symptoms to watch for, the need to avoid certain medications, and the importance of regular followup visits. Sotalol should be initiated in hospital when QTc is ⩾ 450 ms (500 ms with intraventricular conduction delay), HR ⩽60 bpm, or specific risk factors are present (e.g., structural heart disease and renal dysfunction). Hospitalisation is required if QT prolongation occurs or sinus rhythm is not confirmed (risk of sick sinus syndrome or bradycardic pauses). In cases of high proarrhythmic risk (torsades de pointes, syncope, cardiac arrest), inpatient observation is required.

Table 3. **AADs Recommended for Outpatient or Inpatient Initiation [2]**

AAD	In AF		In Sinus Rhythm	
	Inpatient	Outpatient	Inpatient	Outpatient
Class Ia	+		+	
Class Ib			+	+1
Class Ic	+1	+2	+1	+2
Sotalol	+		+	+3
Amiodarone	+1	+2	+1	+2

Notes. [1] – when sinus node function is uncertain or there is a risk of 1:1 AV block;
[2] – when there is potential risk of sinus node dysfunction or AV conduction disturbances;
[3] – when there are no risk markers for AF/AFL and sinus rhythm is present.

To ensure safety and adherence, patients should be educated to recognise potential adverse effects, including palpitations or (pre)syncope during exercise or at rest, which may indicate proarrhythmia. Patients should be informed about possible fooddrug interactions and interactions between QTprolonging drugs.

At each visit, adherence to therapy should be assessed, and risk factors for proarrhythmia should be carefully reviewed. Such a systematic approach ensures effective AAD therapy, allowing therapeutic goals to be achieved without compromising patient safety.

Conclusion

AADs remain a cornerstone of modern therapy for cardiac arrhythmias, despite their modest efficacy and potential for toxic and proarrhythmic effects. Antiarrhythmic drug therapy has traditionally been directed at modulating the generation or propagation of action potentials in the heart using agents acting on membrane ion channels. However, the narrow therapeutic range of AADs complicates their clinical use. For effective and safe treatment of cardiac arrhythmias with AADs, it is necessary to understand the main mechanisms underlying various rhythm disorders, identify the underlying cardiac pathology, consider the pharmacokinetics and antiarrhythmic properties of each individual AAD, adhere to established prescribing guidelines, and carefully monitor the results of pharmacotherapy. Such a comprehensive approach will enable effective and safe medical treatment of cardiac rhythm disorders.

Conflict of interest: none declared.

References

1. Noubiap JJ, Tang JJ, Teraoka JT, et al. Minimum National Prevalence of Diagnosed Atrial Fibrillation Inferred From California Acute Care Facilities. J Am Coll Cardiol. 2024;84(16):1501-1508. DOI: 10.1016/j.jacc.2024.07.014
2. Merino JL, Tamargo J, Blomström-Lundqvist C, et al. Practical compendium of antiarrhythmic drugs: a clinical consensus statement of the European Heart Rhythm Association of the European Society of Cardiology. Europace. 2025;27(8):euaf076. DOI: 10.1093/europace/euaf076
3. Bray JJH, Warraich M, Whitfield MG, et al. Oral class I and III antiarrhythmic drugs for maintaining sinus rhythm after catheter ablation of atrial fibrillation. Cochrane Database Syst Rev. 2023;3(3):CD013765. DOI: 10.1002/14651858.CD013765.pub2
4. Saksena S, Ken-Opurum J, McKindley DS, et al. Arrhythmia Recurrence and Rhythm Control Strategies After Catheter Ablation of Newly Diagnosed Atrial Fibrillation (ARRC-AF Study). JACC Clin Electrophysiol. 2025;11(4):763-775. DOI: 10.1016/j.jacep.2024.11.020
5. Mikhailov EN, Gizatulina TP, Lebedev DS, et al. 2025 Clinical practice guidelines for Ventricular arrhythmias and sudden cardiac death. Russian Journal of Cardiology. 2025;30(11):6670. Russian. DOI: 10.15829/1560-4071-2025-6670
6. Nattel S, Heijman J, Zhou L, Dobrev D. Molecular basis of atrial fibrillation pathophysiology and therapy: a translational perspective. Circ Res. 2020;127(1):51-72. DOI: 10.1161/CIRCRESAHA.120.316363
7. Saljic A, Heijman J, Dobrev D. Recent advances in antiarrhythmic drug therapy. Drugs. 2023;83(13):1147-1160. DOI: 10.1007/s40265-023-01923-3
8. Grandi E, Ripplinger CM. Antiarrhythmic mechanisms of beta blocker therapy. Pharmacol Res. 2019;146:104274. DOI: 10.1016/j.phrs.2019.104274
9. Bottino R, Carbone A, D'Andrea A, et al. Pharmacokinetic determinants for the right dose of antiarrhythmic drugs. Expert Opin Drug Metab Toxicol. 2022;18(3):165-176. DOI: 10.1080/17425255.2022.2046733
10. Lemoine MD, Fabritz L. Improving antiarrhythmic therapy for patients with atrial fibrillation using common genetic variants. Heart. 2025;111(4):145-146. DOI: 10.1136/heartjnl-2024-325242
11. Vaughan Williams EM. Classification of antidysrhythmic drugs. Pharmacol Ther B. 1975;1(1):115-138. DOI: 10.1016/0306-039x(75)90019-7

12. Nattel S. Antiarrhythmic drug classifications. A critical appraisal of their history, present status, and clinical relevance. Drugs. 1991;41(5):672-701. DOI: 10.2165/00003495-199141050-00002
13. Nattel S, Talajic M. Recent advances in understanding the pharmacology of amiodarone. Drugs. 1988;36(2):121-131. DOI: 10.2165/00003495-198836020-00001
14. Chakraborty P, Rose RA, Nair K, et al. The rationale for repurposing funny current inhibition for management of ventricular arrhythmia. Heart Rhythm. 2021;18(1):130-137. DOI: 10.1016/j.hrthm.2020.07.031
15. Bigger JT Jr, Breithardt G, Brown AM, et al. The Sicilian gambit. A new approach to the classification of antiarrhythmic drugs based on their actions on arrhythmogenic mechanisms. Task Force of the Working Group on Arrhythmias of the European Society of Cardiology. Circulation. 1991;84(4):1831-1851. DOI: 10.1161/01.cir.84.4.1831
16. Lei M, Wu L, Terrar DA, Huang CL. Modernized classification of cardiac antiarrhythmic drugs. Circulation. 2018;138(17):1879-1896. DOI: 10.1161/CIRCULATIONAHA.118.035455
17. Chen C, Kaur G, Mehta PK, et al. Ivabradine in cardiovascular disease management revisited: a review. Cardiovasc Drugs Ther. 2021;35(5):1045-1056. DOI: 10.1007/s10557-020-07124-4
18. Li Y, Peng X, Lin R, et al. The Antiarrhythmic mechanisms of flecainide in catecholaminergic polymorphic ventricular tachycardia. Front Physiol. 2022;13:850117. DOI: 10.3389/fphys.2022.850117
19. deSouza IS, Shrestha P, Allen R, et al. Safety and effectiveness of antidysrhythmic drugs for pharmacologic cardioversion of recent-onset atrial fibrillation: a Systematic review and Bayesian network meta-analysis. Cardiovasc Drugs Ther. 2025;39(4):903-923. DOI: 10.1007/s10557-024-07552-6
20. Rillig A, Eckardt L, Borof K, et al. Safety and efficacy of long-term sodium channel blocker therapy for early rhythm control: the EAST-AFNET 4 trial. Europace. 2024;26(6):euae121. DOI: 10.1093/europace/euae121
21. Reiffel JA, Blomström-Lundqvist C, Boriani G, et al. Real-world utilization of the pill-in-the-pocket method for terminating episodes of atrial fibrillation: data from the multinational Antiarrhythmic Interventions for Managing Atrial Fibrillation (AIM-AF) survey. Europace. 2023;25(6):euad162. DOI: 10.1093/europace/euad162
22. Popov SV, Davtyan KV, Shubik YuV, et al. 2025 Clinical practice guidelines for Supraventricular tachycardias. Russian Journal of Cardiology. 2025;30(7):6448. Russian. DOI: 10.15829/1560-4071-2025-6448
23. Zeppenfeld K, Tfelt-Hansen J, de Riva M, et al. 2022 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death. Eur Heart J. 2022;43(40):3997-4126. DOI: 10.1093/eurheartj/ehac262
24. Echt DS, Liebson PR, Mitchell LB, et al. Mortality and morbidity in patients receiving encainide, flecainide, or placebo. The Cardiac Arrhythmia Suppression Trial. N Engl J Med. 1991;324(12):781-788. DOI: 10.1056/NEJM199103213241201
25. Siebels J, Cappato R, Rüppel R, et al. Preliminary results of the Cardiac Arrest Study Hamburg (CASH). CASH Investigators. Am J Cardiol. 1993;72(16):109F-113F. DOI: 10.1016/0002-9149(93)90973-g
26. Boriani G, Mei DA, Imberti JF. Antiarrhythmic drugs in the era of atrial fibrillation ablation. Europace. 2024;26(6):euae122. DOI: 10.1093/europace/euae122
27. Small AJ, Dai M, Halpern DG, Tan RB. Updates in arrhythmia management in adult congenital heart disease. J Clin Med. 2024;13(15):4314. DOI: 10.3390/jcm13154314
28. Kanorskiy S, Shubik Yu. Antiarrhythmic drugs of class Ic in cardiology practice. Vrach. 2025;36(3):32-38. Russian. DOI: 10.29296/25877305-2025-03-06
29. Antzelevitch C, Burashnikov A, Sicouri S, Belardinelli L. Electrophysiologic basis for the antiarrhythmic actions of ranolazine. Heart Rhythm. 2011;8(8):1281-1290. DOI: 10.1016/j.hrthm.2011.03.045
30. Fumagalli S, Dovizio M, Mazzoni S, et al. Ranolazine in patients with chronic coronary syndromes: real-world data provide new evidence on the antiarrhythmic properties of the drug. Eur Heart J Cardiovasc Pharmacother. 2025;11(8):674-681. DOI: 10.1093/ehjcvp/pvaf074
31. Heijman J, Linz D, Schotten U. Dynamics of atrial fibrillation mechanisms and comorbidities. Annu Rev Physiol. 2021;83:83-106. DOI: 10.1146/annurev-physiol-031720-085307
32. Golitsyn SP, Golukhova EZ, Mikhailov EN, et al. 2025 Clinical practice guidelines for atrial fibrillation and flutter. Russian Journal of Cardiology. 2025;30(11):6668. Russian. DOI: 10.15829/1560-4071-2025-6668
33. Karwath A, Bunting KV, Gill SK, et al. Redefining ß-blocker response in heart failure patients with sinus rhythm and atrial fibrillation: a machine learning cluster analysis. Lancet. 2021;398(10309):1427-1435. DOI: 10.1016/S0140-6736(21)01638-X
34. Mujović N, Dobrev D, Marinković M, et al. The role of amiodarone in contemporary management of complex cardiac arrhythmias. Pharmacol Res. 2020;151:104521. DOI: 10.1016/j.phrs.2019.104521
35. Kułakowski P, Karczmarewicz S, Karpiński G, et al. Effects of intravenous amiodarone on ventricular refractoriness, intraventricular conduction, and ventricular tachycardia induction. Europace. 2000;2(3):207-215. DOI: 10.1053/eupc.2000.0099

36. Hamilton D Sr, Nandkeolyar S, Lan H, et al. Amiodarone: a comprehensive guide for clinicians. Am J Cardiovasc Drugs. 2020;20(6):549-558. DOI: 10.1007/s40256-020-00401-5
37. Árpádffy-Lovas T, Husti Z, Baczkó I, et al. Different effects of amiodarone and dofetilide on the dispersion of repolarization between well-coupled ventricular and Purkinje fibers. Can J Physiol Pharmacol. 2021;99(1):48-55. DOI: 10.1139/cjpp-2020-0234
38. Șorodoc V, Indrei L, Dobroghii C, et al. Amiodarone therapy: updated practical insights. J Clin Med. 2024;13(20):6094. DOI: 10.3390/jcm13206094
39. Markman TM, Geng Z, Epstein AE, et al. Trends in antiarrhythmic drug use among patients in the United States between 2004 and 2016. Circulation. 2020;141(11):937-939. DOI: 10.1161/CIRCULATIONAHA.119.044109
40. Kpaeyeh JA Jr, Wharton JM. Sotalol. Card Electrophysiol Clin. 2016;8(2):437-452. DOI: 10.1016/j.ccep.2016.02.007
41. Valembois L, Audureau E, Takeda A, et al. Antiarrhythmics for maintaining sinus rhythm after cardioversion of atrial fibrillation. Cochrane Database Syst Rev. 2019;9(9):CD005049. DOI: 10.1002/14651858.CD005049.pub5
42. Kukendrarajah K, Ahmad M, Carrington M, et al. External electrical and pharmacological cardioversion for atrial fibrillation, atrial flutter or atrial tachycardias: a network meta-analysis. Cochrane Database Syst Rev. 2024;6(6):CD013255. DOI: 10.1002/14651858.CD013255.pub2
43. Pacifico A, Hohnloser SH, Williams JH, et al. Prevention of implantable-defibrillator shocks by treatment with sotalol. d,l-Sotalol Implantable Cardioverter-Defibrillator Study Group. N Engl J Med. 1999;340(24):1855-1862. DOI: 10.1056/NEJM199906173402402
44. Larsen JA, Kadish AH, Schwartz JB. Proper use of antiarrhythmic therapy for reduction of mortality after myocardial infarction. Drugs Aging. 2000;16(5):341-350. DOI: 10.2165/00002512-200016050-00004
45. Godfraind T. Discovery and development of calcium channel blockers. Front Pharmacol. 2017;8:286. DOI: 10.3389/fphar.2017.00286
46. Galyavich AS, Tereshchenko SN, Uskach TM, et al. Russian Journal of Cardiology. 2024 Clinical practice guidelines for chronic heart failure. 2024;29(11):6162. Russian. DOI: 10.15829/1560-4071-2024-6162

DOI: 10.24412/2311-1623-2026-49-19-31

Hypertriglyceridemia in chronic kidney disease: prevalence and clinical spectrum

Murkamilov I.T.[1], Aitbaev K.A.[1], Fomin V.V.[2], Murkamilova Zh.A.[3], Mikhin V.P.[4], Rayimzhanov Z.R.[5], Khakimov Sh.Sh.[6], Solizhonov J.I.[7], Yusupova T.F.[8], Yusupov F.A.[8], Gasanov K.A.[1], Zakirov O.T.[8], Khabibullaev K.K.[1], Ymankulov D.S.[1], Abdibaliev I.A.[1]

[1] Kyrgyz State Medical Academy named after I.K. Akhunbaev, Bishkek, Kyrgyzstan.
[2] Russian Medical Academy of Continuous Professional Education, Moscow, Russia.
[3] Family Medicine Center No. 7, Bishkek, Kyrgyzstan.
[4] Kursk State Medical University, Kursk, Russia.
[5] Main Military Clinical Hospital named after N.N. Burdenko, Moscow, Russia.
[6] Clinical Hospital under the Presidential Affairs Department of the Kyrgyz Republic, Bishkek, Kyrgyzstan.
[7] Republican Specialized Scientific and Practical Medical Center of Nephrology and Kidney Transplantation, Tashkent, Uzbekistan.
[8] Osh State University, Osh, Kyrgyzstan.

AUTHORS

Ilhom T. Murkamilov,* M.D, PhD, Academician of the Russian Academy of Natural Sciences, Kyrgyz State Medical Academy named after I.K. Akhunbaev, Bishkek, Kyrgyzstan. ORCID: 0000-0001-8513-9279

Kubanych A. Aitbaev, M.D, PhD, Professor, Department of Faculty Therapy, Kyrgyz State Medical Academy named after I.K. Akhunbaev, Bishkek, Kyrgyzstan. ORCID: 0000-0003-4973-039X

Viktor V. Fomin, M.D, PhD, Professor, Academician of the Russian Academy of Sciences, Rector, Russian Medical Academy of Continuous Professional Education, Moscow, Russia. ORCID: 0000-0002-2682-4417

Zhamila A. Murkamilova, General Practitioner, Researcher, Family Medicine Center No. 7, Bishkek, Kyrgyzstan. ORCID: 0000-0002-7653-0433

Vadim P. Mikhin, M.D, PhD, Professor, Head of the Department of Internal Medicine No. 2, Kursk State Medical University, Kursk, Russia. ORCID: 0000-0002-5398-9727

Zafarbek R. Rayimzhanov, Neurologist, Neurological Department No. 29, Main Military Clinical Hospital named after N.N. Burdenko, Moscow, Russia. ORCID: 0000-0001-5746-6731

Shavkatjon Sh. Khakimov, Intensive Care Physician, Researcher, Clinical Hospital under the Presidential Affairs Department of the Kyrgyz Republic, Bishkek, Kyrgyzstan. ORCID: 0009-0004-0437-0188

Jaloliddin I. Solizhonov, Clinical Resident, Republican Specialized Scientific and Practical Medical Center of Nephrology and Kidney Transplantation, Tashkent, Uzbekistan. ORCID: 0009-0003-0078-0609

* Corresponding author. Tel.: +996557221983. E-mail: murkamilov.i@mail.ru

Tursunoy F. Yusupova, Clinical Resident, Department of Neurology, Medical Rehabilitation and Mental Health, Faculty of Medicine, Osh State University, Osh, Kyrgyzstan. ORCID: 0000-0002-8502-2203
Furkat A. Yusupov, M.D, PhD, Professor, Head of the Department of Neurology, Medical Rehabilitation and Mental Health, Faculty of Medicine, Osh State University, Osh, Kyrgyzstan. ORCID: 0000-0003-0632-6653
Kamranbey A. Gasanov, Clinical Resident, Department of Neurology and Clinical Genetics, Kyrgyz State Medical Academy named after I.K. Akhunbaev, Bishkek, Kyrgyzstan. ORCID: 0000-0003-0173-8851
Omurbek T. Zakirov, Assistant, Department of Neurology, Medical Rehabilitation and Mental Health, Faculty of Medicine, Osh State University, Osh, Kyrgyzstan. ORCID: 0000-0003-0632-6653
Komiljon K. Khabibullaev, Research Physician, Kyrgyz State Medical Academy named after I.K. Akhunbaev, Bishkek, Kyrgyzstan. ORCID: 0009-0004-5508-8019
Daniyar S. Ymankulov, Research Physician, Kyrgyz State Medical Academy named after I.K. Akhunbaev, Bishkek, Kyrgyzstan. ORCID: 0009-0000-4975-1196
Ibadilla A. Abdibaliev, Research Physician, Kyrgyz State Medical Academy named after I.K. Akhunbaev, Bishkek, Kyrgyzstan. ORCID: 0009-0002-0921-0410

Aim. To determine the prevalence of hypertriglyceridemia (HTG) and evaluate its association with markers of renal dysfunction in chronic kidney disease (CKD).

Material and methods. The study utilized clinical, laboratory, and instrumental data from 562 patients with non-diabetic CKD. The mean age of patients was 37.7 years (age range 17 to 72 years). Anthropometric, hemodynamic, and laboratory parameters were assessed. Patients were divided into two groups: Group 1 — women (n=185), Group 2 — men (n=377). A blood triglyceride (TG) concentration of ⩾ 1.7 mmol/L was considered as HTG.

Results. In the overall cohort of CKD patients, the prevalence of HTG was 55.3%. The frequency of HTG was higher at CKD stages 3B (72.00%), 3A (67.20%), 2 (60.90%), and 1 (57.50%) compared to stages 4 (49.20%) and 5 (39.50%). Levels of systolic, diastolic, pulse, and mean arterial pressure (MAP), as well as 24-hour proteinuria, were significantly higher, while high-density lipoprotein cholesterol (HDL-C) levels were significantly lower in men than in women. Lower values of peripheral blood laboratory parameters (hemoglobin, red blood cells, platelets) and nitrogen excretion function of the kidneys were characteristic of females. A strong correlation was found between estimated glomerular filtration rate (eGFR) and risk factors for chronic renal failure in both female and male patients. In the female CKD group, eGFR significantly correlated with age, systolic, diastolic and mean arterial pressure, hemoglobin (Hb) concentration, red blood cell and platelet counts. In men with CKD, eGFR significantly correlated with age, systolic, diastolic, pulse and mean arterial pressure, Hb concentration, red blood cell and platelet counts, as well as serum total cholesterol, HDL-C, and TG levels. In the overall patient cohort, a statistically significant relationship was observed between serum TG concentration and both eGFR and 24-hour proteinuria.

Conclusion. In patients with CKD, HTG is more common at the stage of renal insufficiency and is closely associated with markers of renal dysfunction. The association of HTG with cardiovascular risk factors is more pronounced in men. These findings highlight the need for early screening of triglyceride levels for timely correction of metabolic disorders and slowing the progression of chronic kidney disease. A differentiated approach to lipid profile assessment in men and women will allow for more accurate prediction of disease course and optimization of preventive therapy strategies.

Keywords: chronic kidney disease, hypertriglyceridemia, risk factors, chronic renal failure, prognosis, healthcare.

Conflict of Interest: none declared.

Received: 22.03.2026
Accepted: 20.05.2026

For citation: Murkamilov IT, Aitbaev KA, Fomin VV, et al. Hypertriglyceridemia in chronic kidney disease: prevalence and clinical spectrum. International Heart and Vascular Disease Journal. 2026; 14(50): 16-26. DOI: 10.24412/2311-1623-2026-50-19-31

DOI: 10.24412/2311-1623-2026-49-19-31

Introduction

Patients with chronic kidney disease (CKD) belong to the high and very high cardiovascular risk (CVR) groups. The study of the role of non-immune factors in the development of cardiovascular disorders and the progression of CKD represents an important area of modern preventive medicine [1, 2]. A blood triglyceride (TG) concentration of ≥1.7 mmol/L is defined as hypertriglyceridemia (HTG) [3], which is widespread among patients with CKD. According to research data, HTG is accompanied by decreased lipoprotein clearance, increased concentrations of very low-density lipoproteins (VLDL), and accumulation of intermediate-density lipoproteins [3, 4]. Possible mechanisms of renal HTG include changes in enzyme expression and/or activity, impaired receptor apparatus function, and reduced high-density lipoprotein metabolism [5]. At the stage of chronic renal failure (CRF), insulin resistance is observed, which contributes to increased VLDL production in the liver and partially explains the development of HTG [3, 5]. Additionally, decreased lipase activity leads to impaired breakdown of TGs into free fatty acids necessary for the body's energy supply, which may also contribute to increased CVR.

Numerous studies have shown that HTG, in combination with other CVR factors, contributes to an increased frequency of cardiovascular events and the progression of CRF [6, 7]. Elevated blood TG concentrations in CKD, especially at the CRF stage, have specific features compared to the general population. For example, within the ARIC (Atherosclerosis Risk in Communities) registry, it was established that an increase in TG levels is accompanied by the progression of renal dysfunction [8]. Subsequent studies confirmed the contribution of HTG to the development of coronary artery disease (CAD), which is common in patients with CKD [9]. In one previously published study, it was shown that at TG concentrations >1.6 mmol/L, the incidence of CAD reaches 11.5% [10]. According to a meta-analysis by foreign colleagues, HTG is considered an independent risk factor (RF) for CAD: an increase in TG levels by 1.0 mmol/L is associated with a 32% increase in the risk of cardiovascular disease (CVD) in men and 76% in women [11]. Studies from the last five years have also demonstrated a link between elevated TG concentrations and a number of other pathologies, including arterial hypertension (AH), preeclampsia, cerebral ischemia, and acute pancreatitis [12].

Aim of the study. To determine the frequency of HTG and assess its relationship with markers of renal dysfunction in CKD.

Materials and methods

The study used clinical, laboratory, and instrumental data from patients with CKD due to chronic glomerulonephritis (without morphological verification) who underwent inpatient treatment in the nephrology department of the National Center of Cardiology and Therapy named after Academician Mirsaid Mirrakhimov between September 2008 and September 2016. This study is an observational, cross-sectional (retrospective) study conducted in accordance with the principles of the Declaration of Helsinki. All patients signed informed voluntary consent to participate. Inclusion criterion: presence of glomerular and tubulointerstitial kidney diseases.

Exclusion criteria: type 1 and type 2 diabetes mellitus (DM), AH, heart failure of functional class III–IV, hypothyroidism, systemic connective tissue diseases, gout, polycystic ovary syndrome, pregnancy and lactation, as well as patients receiving scheduled hemodialysis.

The analysis included 562 patients with an established diagnosis of chronic kidney disease. The mean age of the participants was 37.7 ± 12.7 years (range: 17 to 72 years).

Anthropometric parameters were recorded for all patients: height, body weight, and body mass index (BMI), with the determination of overweight (OW) and the degree of obesity. Systolic and diastolic blood pressure (SBP and DBP) were measured, mean and pulse pressure were calculated, and heart rate (HR) was recorded.

The laboratory part of the study included determination of hemoglobin (Hb) levels, erythrocyte and platelet counts, and erythrocyte sedimentation rate (ESR). Lipid profile analysis included determination of total cholesterol (TC), TGs, low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C). Additionally, venous blood creatinine and glucose concentrations were measured.

The nitrogen-excretory function of the kidneys was assessed by estimated glomerular filtration rate (eGFR), calculated using the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) formula. Daily proteinuria was also measured in all patients.

In accordance with Russian and international clinical guidelines, the following CVR factors were identified: OW (BMI 25.0–29.9 kg/m²); grade I obesity (BMI 30.0–34.9 kg/m²); grade II obesity (BMI 35.0–39.9 kg/m²); grade III obesity (BMI ⩾40 kg/m²) [13]; systolic AH (SBP ⩾140 mm Hg); diastolic AH (diastolic BP ⩾90 mm Hg); tachycardia (resting HR ⩾80 beats/min) [14]; renal failure (eGFR <60 ml/min); nephrotic proteinuria (daily proteinuria >3.5 g); anemia (Hb <120 g/L in women and <130 g/L in men); HTG (TG ⩾1.7 mmol/L); hypercholesterolemia (TC >5.01 mmol/L) [1]. CKD stages were determined according to the recommendations of the Scientific Society of Nephrologists of Russia, published in 2021 [15].

The examined patients with CKD were divided into two groups: group 1 — women (n=185); group 2 — men (n=377). The groups were comparable in age: 38.7 ± 11.9 years and 37.2 ± 13.0 years, respectively (p=0.166).

Statistical analysis

Statistical data processing was performed using Microsoft Excel spreadsheets and the Statistica 10.0 software package. Qualitative characteristics are presented as absolute and relative values (n, %). Continuous variables were described as median (Me) and interquartile range [Q25; Q75] for non-parametric distribution, or as mean (M) and standard deviation (SD) for normal distribution.

Student's t-test was used to compare quantitative indicators between the two groups. The Mann–Whitney U-test was used for independent samples. Correlation analysis was performed using Pearson's correlation coefficient to assess relationships. The critical significance level for testing the null hypothesis was set at $p < 0.05$.

Results

According to the analysis results (Fig. 1), the majority of examined patients were at early stages of CKD: C1 (n=146) and C2 (n=110). The number of patients at later stages was: C3A — 58, C3B — 50, C4 — 56, and C5 — 129 individuals.

The number of women and men at CKD stages was: C1 — 31 and 115; C2 — 42 and 68; C3A — 24 and 34; C3B — 16 and 34; C4 — 24 and 45; C5 — 48 and 81, respectively. Among the examined patients, signs of CRF, i.e., a decrease in eGFR <60 ml/min, were observed in 306 (54.4%) individuals.

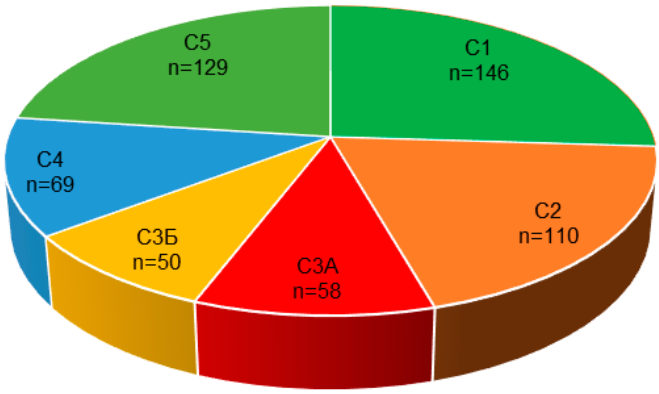

Fig. 1. Distribution of the examined patients with CKD

Table 1 presents the indicators of nitrogen-excretory renal function (median and interquartile range), daily proteinuria, and blood lipid spectrum parameters. According to these data, the examined patients had an initial stage of CRF (serum creatinine — 131.0 μmol/L, eGFR — 52.7 ml/min).

Proteinuria was characterized by a predominance of nephrotic variants of CKD (2.256 g/day). Blood lipid spectrum levels corresponded to the criteria for hyperlipidemia and dyslipidemia.

Table 1. **Characteristics of renal function and blood lipid spectrum in the examined patients with CKD, n=562**

Parameters	Me (Q25; Q75)
Serum creatinine, μmol/L	131.0 (87,0; 347,0)
eGFR, ml/min	52.7 (17.0; 91.5)
Daily proteinuria, g/day	2.256 (0.859; 4.817)
TC, mmol/L	5.27 (4.10; 6.70)
TG, mmol/L	1.81 (1.14; 2.57)
LDL-C, mmol/L	3.19 (2.35; 4.54)
HDL-C, mmol/L	1.00 (0.80; 1.30)

In accordance with the study objectives, a comparative analysis of clinical and laboratory data was performed (Table 2). The patient groups did not differ significantly in age, BMI, heart rate, fasting venous blood glucose, TC, LDL-C, TG, or creatinine levels.

In men, the values of systolic (144 ± 27 mm Hg vs. 137 ± 25 mm Hg, p=0.001), diastolic (91 ± 15 mm Hg vs. 88 ± 16 mm Hg, p=0.014), pulse (53 ± 17 mm Hg vs. 49 ± 17 mm Hg, p=0.001), and mean (48 ± 9 mm Hg vs. 45 ± 8 mm Hg, p=0.001) blood pressure, as well as daily proteinuria (2.542 [0.871; 5.566] g vs. 1.947 [0.781; 3.958] g, p=0.033), were statistically significantly higher, while HDL-C levels (1.04 ± 0.42 mmol/L

DOI: 10.24412/2311-1623-2026-49-19-31

Table 2. **Comparative characteristics of patients included in the study, n=562**

Parameter	Women with CKD, n=185	Men with CKD, n=377	p
Mean age, years	38.7±11.9	37.2±13.0	0.166
BMI, kg/m²	26.6±6.0	25.9±6.1	0.182
SBP, mm Hg	137±25	144±27	0.001
DBP, mm Hg	88±16	91±15	0.014
Pulse pressure, mm Hg	49±17	53±17	0.001
Mean BP, mm Hg	45±8	48±9	0.001
HR, beats/min	77±10	76±9	0.291
Hemoglobin, g/L	116.3±25.1	133.5±28.2	0.001
Erythrocytes, ×10¹²/L	4.03±0.62	4.39±0.64	0.001
Platelets, ×10⁹/L	233.6±25.9	245.1±25.0	0.001
ESR, mm/h	16.0 (10.0;28.0)	12.0 (5.0;24.5)	0.001
Glucose, mmol/L	4.76±0.78	4.71±1.08	0.642
TC, mmol/L	5.31 (4.24;6.42)	5.23 (4.07;6.80)	0.796
HDL-C, mmol/L	1.18±0.43	1.04±0.42	0.001
LDL-C, mmol/L	3.19 (2.42;4.27)	3.19 (2.32;4.63)	0.661
TG, mmol/L	1.82 (1.18;2.25)	1.78 (1.14;2.62)	0.383
Creatinine, μmol/L	129.5 (82.0;341.0)	131.6 (88.0;347.0)	0.309
eGFR, ml/min	46.5 (14.3;80.9)	57.5 (17.9;96.4)	0.013
Proteinuria, g/day	1.947 (0.781;3.958)	2.542 (0.871;5.566)	0.033

vs. 1.18 ± 0.43 mmol/L, p=0.001) were significantly lower compared to women.

In women, on the contrary, lower values of Hb (116.3 ± 25.1 g/L vs. 133.5 ± 28.2 g/L, p=0.001), erythrocyte count (4.03 ± 0.62 × 10^{12}/L vs. 4.39 ± 0.64 × 10^{12}/L, p=0.001), platelet count (233.6 ± 25.9 × 10^9/L vs. 245.1 ± 25.0 × 10^9/L, p=0.001), and eGFR (46.5 [14.3; 80.9] ml/min vs. 57.5 [17.9; 96.4] ml/min, p=0.013) were observed. At the same time, the ESR in women was statistically significantly higher (16.0 [10.0; 28.0] mm/h vs. 12.0 [5.0; 24.5] mm/h, p=0.001) compared to men with CKD.

A comparative analysis of CKD-associated risk factors for renal failure in women and men showed that the frequency of overweight (28.6% and 31.2%), grade I obesity (12.4% and 13.7%), grade II obesity (8.1% and 4.2%), grade III obesity (4.3% and 1.3%), diastolic hypertension (49.1% and 58.6%), tachycardia (34.5% and 26.2%), hypercholesterolemia (57.2% and 53.0%), HTG (58.3% and 53.0%), and nephrotic proteinuria (29.7% and 39.2%) did not differ significantly between the groups (Table 3).

As expected, the prevalence of anemia (51.3% and 38.9%, p<0.05) and CRF (83.2% and 69.4%, p<0.05) was statistically significantly higher in women compared to men. Overall, among the 562 patients with CKD, HTG was present in 311 individuals, accounting for 55.3% of cases.

Figure 2 presents the frequency of HTG in patients with CKD depending on the stage of the disease. The

Table 3. **Characteristics of risk factors in the examined patients, n=562**

Parameter	Women with CKD, n=185	Men with CKD, n=377
Overweight, n	53 (28.6%)	118 (31.2%)
Grade I obesity, n	23 (12.4%)	52 (13.7%)
Grade II obesity, n	15 (8.1%)	16 (4.2%)
Grade III obesity, n	8 (4.3%)	5 (1.3%)
Systolic hypertension, n	90 (48.6%)	226 (59.9%)*
Diastolic hypertension, n	91 (49.1%)	221 (58.6%)
Increased HR, beats/min, n	64 (34.5%)	99 (26.2%)
Anemia, n	95 (51.3%)*	147 (38.9%)
Hypercholesterolemia, n	106 (57.2%)	200 (53.0%)
HTG, n	108 (58.3%)	203 (53.8%)
CRF, n	154 (83.2%)*	262 (69.4%)
Nephrotic proteinuria, n	55 (29.7%)	148 (39.2%)

Note. * — p < 0.05 (statistically significant differences between men and women).

frequency of HTG at stages C3B (72%), C3A (67.2%), C2 (60.9%), and C1 (57.5%) was higher than at the later C4 and C5 stages (49.2% and 39.5%, respectively).

Additionally, blood TG concentrations in patients with CKD were assessed depending on the disease stage (Fig. 3). Statistically significantly higher TG levels were observed at stages C3A (2.20 [1.45; 3.05] mmol/L) and C3B (2.01 [1.52; 2.63] mmol/L) compared to stages C1 (1.84 [1.12; 2.62] mmol/L), C2 (1.91 [1.15; 2.82] mmol/L), C4 (1.60 [1.08; 2.57] mmol/L), and C5 (1.35 [0.89; 1.89] mmol/L).

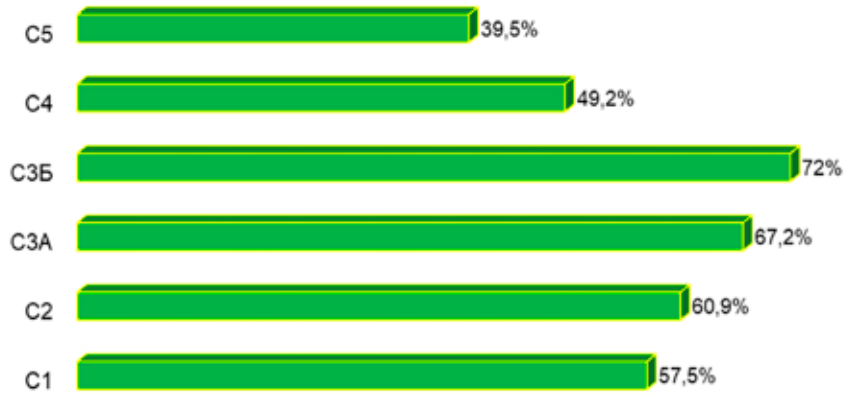

Fig. 2. Frequency of HTG in patients with CKD

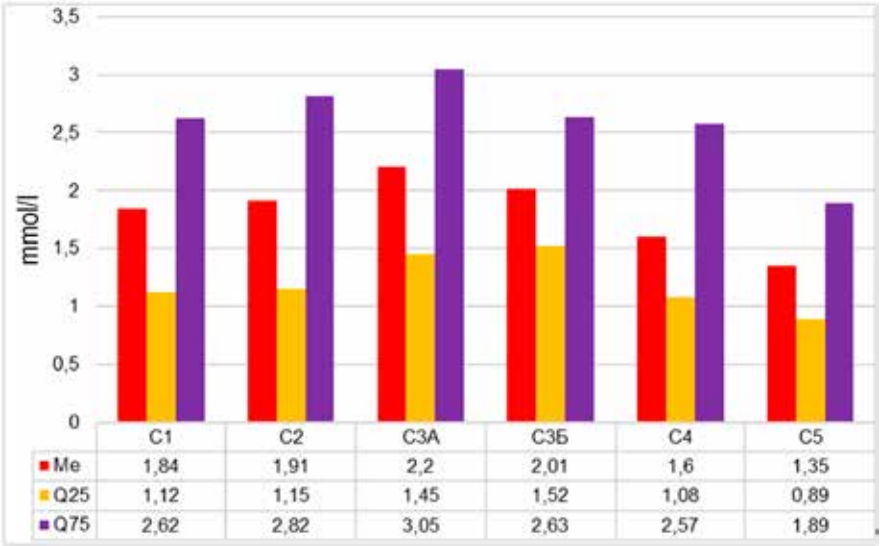

Fig. 3. Blood TG concentration in patients with CKD

Table 4. **Correlation of eGFR with clinical and laboratory data in the examined patients with CKD**

Parameter	Women with CKD, n=185		Men with CKD, n=377	
	eGFR, ml/min			
	r	p	r	p
Mean age, years	0.464	0.001	0.305	0.001
BMI, kg/m²	0.037	0.717	0.073	0.239
SBP, mm Hg	0.223	0.023	0.579	0.001
DBP, mm Hg	0.253	0.010	0.429	0.001
Pulse pressure, mm Hg	0.153	0.171	0.547	0.001
Mean BP, mm Hg	0.223	0.023	0.579	0.001
HR, beats/min	0.024	0.806	0.032	0.607
Hemoglobin, g/L	-0.46	0.001	-0.570	0.001
Erythrocytes, ×10¹²/L	-0.451	0.001	-0.567	0.001
Platelets, x109/L	-0.265	0.001	-0.446	0.001
ESR, mm/h	0.123	0.227	0.103	0.150
Glucose, mmol/L	0.074	0.464	0.119	0.096
TC, mmol/L	0.126	0.213	0.246	0.001
HDL-C, mmol/L	-0.171	0.092	-0.297	0.001
LDL-C, mmol/L	0.131	0.198	0.058	0.443
TG, mmol/L	0.143	0.147	0.103	0.046

Table 4 presents the results of the correlation analysis of eGFR with risk factors for CRF in women and men.

In the group of women with CKD, eGFR correlated significantly with age (r = 0.464; p = 0.001), systolic (r = 0.223; p = 0.023), diastolic (r = 0.253; p = 0.010), and mean (r = 0.223; p = 0.023) blood pressure, Hb concentration (r = 0.460; p = 0.001), erythrocyte count (r = 0.451; p = 0.001), and platelet count (r = 0.265; p = 0.001).

In men with CKD, eGFR also correlated significantly with age (r = 0.305; p = 0.001), systolic (r = 0.579; p = 0.001), diastolic (r = 0.429; p = 0.001), pulse (r = 0.547; p = 0.001), and mean (r = 0.579; p = 0.001) blood pressure, Hb concentration (r = 0.570; p = 0.001), erythrocyte count (r = 0.567; p = 0.001), and platelet count (r = 0.446; p = 0.001), as well as with TC (r = 0.246; p = 0.001), HDL-C (r = 0.297; p = 0.001), and TG (r = 0.103; p = 0.046).

DOI: 10.24412/2311-1623-2026-49-19-31

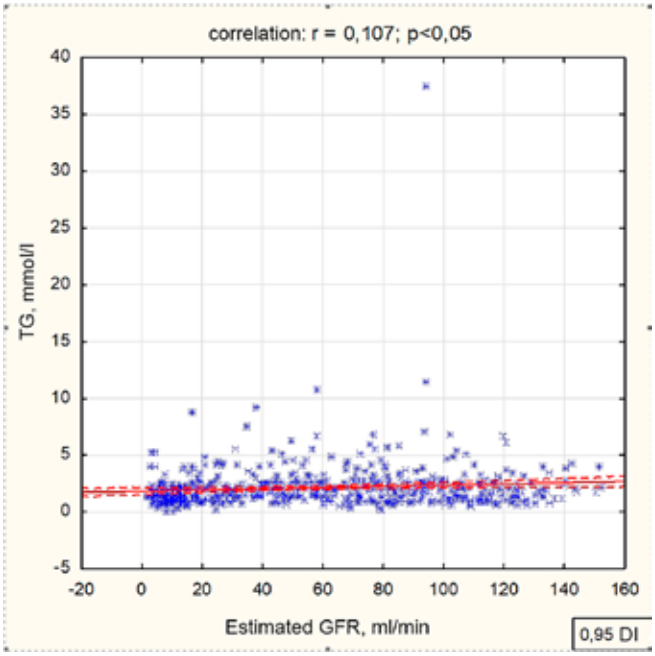

Fig. 4. Correlation of blood triglyceride concentration with eGFR in patients with CKD in the overall group

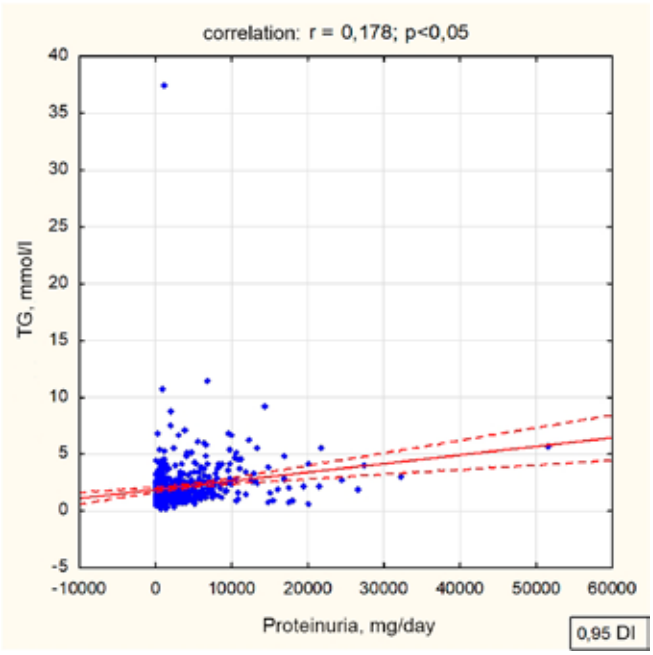

Fig. 5. Correlation of blood TG concentration with daily proteinuria in patients with CKD in the overall group

Given the absence of a statistically significant correlation between TG concentration and eGFR in the group of women, an additional assessment of the relationship between these parameters was performed in the overall sample. According to the data presented in Figures 4 and 5, TG concentration was statistically significantly correlated with eGFR ($r = 0.17$; $p < 0.05$) and daily proteinuria ($r = 0.178$; $p < 0.05$).

Discussion

Hypertriglyceridemia is frequently detected in patients with CKD, manifesting as an elevation of serum TG levels above reference values and associated with increased cardiovascular risk [15, 16]. Nephrogenic HTG is secondary in nature and is considered an indicator of the activity of the pathological process in the kidneys. Blood TG concentration particularly increases in the presence of nephrotic proteinuria and dysproteinemia, which are characteristic of early stages of CKD. In our study, the majority of patients were at the initial stage of CKD and had signs of early CRF.

The mechanisms of HTG formation in patients with CKD, especially in proteinuric variants, are complex and diverse. According to the literature, enhanced mobilization of free fatty acids from peripheral adipose tissue to the liver leads to increased concentrations of LDL and TG-enriched lipoproteins [17]. Additionally, in CKD, there is a decrease in lipoprotein lipase activity, a key enzyme responsible for the hydrolysis of TG-containing lipoproteins. As a result, patients with CKD and concomitant HTG exhibit reduced HDL-C levels and elevated LDL-C levels [15]. As shown in the present study, men with CKD were characterized by significantly higher blood pressure values, daily proteinuria, and lower HDL-C levels.

According to the literature, in the general population, blood TG levels are higher in men than in women, especially under the age of 70 [16]. The prevalence of HTG in the general population exceeds 10%, which is comparable to the frequency of CKD and type 2 diabetes mellitus [18]. In one study, the frequency of HTG in individuals with hypertension was 34.34% [19]. According to the NHANES (3rd National Health and Nutrition Examination Survey) registry, the prevalence of HTG among patients with CVD reaches 62% [20]. Previously published studies have noted that the frequency of HTG is higher among Mexican Americans compared to White Americans, while it was significantly lower in African Americans [21]. In our study, the prevalence of HTG among patients with CKD was 55.3%. According to other data, the frequency of HTG among individuals with CVD reaches 62% in Europe and 29.2% in the Russian Federation [22]. In our study, a high prevalence of HTG was identified at CKD stages C3B (72%), C3A (67.2%), C2 (60.9%), and C1 (57.5%). The median TG concentration was signifi-

cantly higher in patients with stage C3 CKD. It should be noted that the median and interquartile TG levels did not differ significantly between women and men.

With age, the frequency of HTG increases, reaching a maximum at 55–65 years, which is explained by the age-related increase in the incidence of type 2 diabetes mellitus, CKD, and CAD. In the present study, the median blood TG level was 1.81 mmol/L. It is known that in the general population, HTG is associated with hypertension, hypercholesterolemia, and atherogenic dyslipidemia. These data are fully reflected in our study. The results of a recent study allow us to identify a causal relationship between changes in blood lipid spectrum parameters and increased blood pressure [23]. In this regard, it can be assumed that elevated blood pressure is closely related to HTG, and their combination contributes to the development of renal dysfunction.

At the molecular-cellular level, elevated TG concentrations are associated with key manifestations of endothelial dysfunction, including impaired vasodilation, enhanced production of chemokines and cytokines, activation of the inflammatory response, and monocyte infiltration in renal tissue [24, 25]. These processes contribute to increased proteinuria and increase the risk of CRF progression. In our study group, the median values of serum creatinine and eGFR corresponded to the criteria for the initial stage of CRF. According to the literature, in CKD, the frequency of HTG increases as nitrogen-excretory renal function declines [26, 27]. In our previously published studies, we demonstrated a high prevalence of HTG among individuals with various cardiovascular risk categories [28], as well as an association between TG concentration and risk factors for CRF in patients with comorbid pathology [29].

According to the data of the present study, HTG is associated with the progression of CRF in CKD, especially in men. This is confirmed by a statistically significant correlation between elevated blood TG concentrations and decreased eGFR. It is likely that the presence of HTG in CKD exerts a synergistic effect on cardiovascular risk factors, as several studies have shown that the combination of elevated blood pressure with HTG increases the risk of all-cause mortality by 2.8 times [30].

On the other hand, the involvement of peripheral blood platelets in atherogenesis is an established fact. Under conditions of HTG, platelet aggregation and thrombus formation are enhanced [31], which potentiates the thrombotic component of atherogenesis and may contribute to the progression of vascular and renal complications. In this regard, the statistically significant association between platelet count and eGFR in both women and men, demonstrated in our study, logically fits into the pathophysiological model where platelet activation in the context of HTG contributes to a greater decline in eGFR through microvascular mechanisms.

The active involvement of TG-rich particles in atherosclerotic processes is explained by their ability to be readily taken up by macrophages migrating into the vascular wall [32]. TG accumulation in macrophages enhances the synthesis of reactive oxygen species, contributing to foam cell formation [33] and accelerating the development of atherosclerotic changes. Additionally, under conditions of HTG, increased vascular endothelial permeability is observed [34], making it more vulnerable to damage. When HTG is combined with anemia, hypertension, or electrolyte imbalance, the risk of endothelial cell damage and death increases significantly, which is accompanied by the progression of endothelial dysfunction, the development of CRF, and an increased frequency of cardiovascular events.

It should be emphasized that HTG in CKD has dual pathobiological significance: on the one hand, it contributes to the development of renal dysfunction and the progression of CRF, and on the other hand, it creates prerequisites for the occurrence of cardiovascular events [35]. The results of the correlation analysis presented in Figures 4 and 5 confirm the role of HTG in the development of renal dysfunction and the progression of CRF. In a prospective cohort study by Russian colleagues, it was shown that the presence of HTG increases the relative risk of cardiovascular mortality by 2.15 times. The authors note that HTG was found to be a significant risk factor for mortality exclusively in women [30].

Summarizing the accumulated research findings, it should be emphasized that a TG level >2.3 mmol/L is considered a risk factor for the development of CVD, for which pharmacological therapy is recommended [36, 37]. For patients with CVD and CKD, a TG level of < 1.7 mmol/L is considered the target, reflecting the need for strict lipid profile control in this group. These clinical benchmarks confirm that HTG acts not only as an independent risk factor but also as an element of a complex pathogenetic system that in-

teracts with other unfavorable factors. It follows that there is a close clinical and pathogenetic interrelationship between the studied cardiovascular risk factors, which represent not a simple sum of individual effects but possess a synergistic, mutually reinforcing impact on the progression of CRF and cardiovascular complications.

Conclusion

The results of the present study demonstrate a high prevalence of HTG in CKD at early stages of CRF. In both women and men with CKD, HTG is associated with hypertension, tachycardia, anemia, and reduced nitrogen-excretory renal function. The identified associations of HTG with cardiovascular risk factors and renal dysfunction underscore the need for early assessment of blood TG levels in patients with CKD, which will allow timely enhancement of therapeutic and preventive measures at the outpatient stage.

Thus, the obtained data confirm that HTG in CKD, especially in men, should be considered a priority target for the prevention of cardiovascular events and improvement of prognosis in this patient population.

Conflict of Interest: none declared.

References

1. Drapkina OM, Kobalava ZhD, Shestakova MV, et al. Cardiovascular risk and chronic kidney disease: strategies for cardiac and renal protection. Interdisciplinary consensus. Cardiovascular Therapy and Prevention. 2025;24(6):44-66. Russian. DOI:10.15829/1728-8800-2025-4466
2. Drapkina OM, Mazurov VI, Martynov AI, et al. Consensus statement on the management of patients with asymptomatic hyperuricemia in general medical practice. Cardiovascular Therapy and Prevention. 2024;23(1):89-104. Russian. DOI:10.15829/1728-8800-2024-3737
3. Ezhov MV, Kukharchuk VV, Sergienko IV, et al. Disorders of lipid metabolism. Clinical Guidelines 2023. Russian Journal of Cardiology. 2023;28(5):54-71. Russian. DOI:10.15829/1560-4071-2023-5471
4. Blumenthal RS, Morris PB, Gaudino M, et al. 2026 ACC/AHA/AACVPR/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Dyslipidemia: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. J Am Coll Cardiol. 2026; 13:S0735-1097(25)10254-4. DOI:10.1016/j.jacc.2025.11.016
5. Tramontano D, D'Erasmo L, Larouche M, et al. The vicious circle of chronic kidney disease and hypertriglyceridemia: What is first, the hen or the egg? Atherosclerosis. 2025; 403:119146. DOI:10.1016/j.atherosclerosis.2025.119146
6. Ovwasa H, Aiwuyo HO, Okoye OA, et al. Risk Assessment of Pre-dialysis Chronic Kidney Disease (CKD) Patients for Cardiovascular Disease (CVD) in a Tertiary Hospital in Nigeria: A Case-Controlled Cross-Sectional Study. Cureus. 2023; 27;15(3):e36725. DOI:10.7759/cureus.36725
7. Wang Z, Deng X, Yang Z, et al. Association between cardiovascular-kidney-metabolic health metrics and long-term cardiovascular risk: Findings from the Chinese Multi-provincial Cohort Study. Chin Med J (Engl). 2025; 5;138(17):2139-2147. DOI:10.1097/CM9.0000000000003752
8. Hussain A, Sun C, Selvin E, et al. Triglyceride-rich lipoproteins, apolipoprotein C-III, angiopoietin-like protein 3, and cardiovascular events in older adults: Atherosclerosis Risk in Communities (ARIC) study. Eur J Prev Cardiol. 2022 Mar 11;29(2):e53-e64. DOI:10.1093/eurjpc/zwaa152
9. Konnov M.V., Deev A.D. Own and Parental Predictors of Hypertriglyceridemia in Children of Persons with Early Ischemic Heart Disease. Cardiology. 2019;59(7):11-18. Russian. DOI:10.18087/cardio.2019.7.10266
10. Siegel PM, Katzmann JL, Weinmann-Menke J, et al. A practical guide to the management of dyslipidaemia. Clin Res Cardiol. 2026; 115(2):185-197. DOI:10.1007/s00392-025-02833-y
11. Li Z, Wu Y, Yang Y, et al. Prognostic effect of triglyceride glucose-related parameters on all-cause and cardiovascular mortality in individuals with cardiovascular-kidney-metabolic syndrome: evidence from international multi-cohort studies. Cardiovasc Diabetol. 2026; 19;25(1):42. DOI:10.1186/s12933-025-03057-0
12. Arabidze GG, Mamedov MN, Polyakova OV, Akhundova KhR Update of ESC/EAS 2025 Recommendations on the Management of Patients with Dyslipidemias. Effective Pharmacotherapy. 2025; 21 (34): 6–16. Russian. DOI:10.33978/2307-3586-2025-21-34-6-16
13. Dedov II, Mokrysheva NG, Melnichenko GA, et al. Clinical recommendations «Gestational diabetes mellitus» of the Russian Ministry of Health. Version of the year 2024. Bulletin of Reproductive Health. 2025;4(2):14-30. Russian. DOI:10.14341/brh12763
14. Kobalava ZhD, Konradi AO, Nedogoda SV, et al. 2024 Clinical practice guidelines for Hypertension in adults. Russian Journal of Cardiology. 2024;29(9):6117. Russian. DOI:10.15829/1560-4071-2024-6117

15. Clinical recommendations. Chronic kidney disease (CKD). Nephrology (Saint-Petersburg) 2021;25(5):10-82. Russian. DOI:10.36485/1561-6274 2021-25-5-10-8
16. Obrezan AG, Serezhina EK, Shomin AV Hypertriglyceridemia. Aspects of epidemiology and etiopathogenesis (literature review). Cardiology: News, Opinions, Training.2023;11(4):14-21. Russian. DOI:10.33029/2309-1908-2023-11-4-14-21
17. Baek J, He C, Afshinnia F, Michailidis G, Pennathur S. Lipidomic approaches to dissect dysregulated lipid metabolism in kidney disease. Nat Rev Nephrol. 2022; 18(1):38-55. DOI:10.1038/s41581-021-00488-2
18. Bubnova MG, Ezhov MN, Aronov DM, et al. Hypertriglyceridemia (triglyceride-rich lipoproteins and their remnants): role in the development of atherosclerotic cardiovascular diseases and control strategy. Opinion of the Expert Committee of the Russian Society of Cardiology, the National Atherosclerosis Society, and the Russian Society of Cardiac and Somatic Rehabilitation and Secondary Prevention. Russian Journal of Cardiology. 2025;30(5):6364. Russian. DOI:10.15829/1560-4071-2025-6364
19. Wang Y, Wei N, Li M, et al. Association between the triglyceride-glucose-frailty index and all-cause and cardiovascular mortality in individuals with cardiovascular-kidney-metabolic syndrome: the mediating role of the poverty-income ratio. Cardiovasc Diabetol. 2026; 25(1):58. DOI:10.1186/s12933-026-03076-5
20. Kim H, Hu EA, Rebholz CM. Ultra-processed food intake and mortality in the USA: results from the Third National Health and Nutrition Examination Survey (NHANES III, 1988-1994). Public Health Nutr. 2019; 22(10):1777-1785. DOI:10.1017/S1368980018003890
21. Cabodevilla AG, Izquierdo MC, Basu D, et al. Non-remnant triglyceride-rich lipoproteins due to lipoprotein lipase deficiency increase atherosclerosis in mice. Nat Commun. 2026 Jan 3;17(1):1458. DOI:10.1038/s41467-025-68193-3
22. Karpov Y, Khomitskaya Y. PROMETHEUS: an observational, cross-sectional, retrospective study of hypertriglyceridemia in Russia. Cardiovasc Diabetol. 2015; 25;14:115. DOI:10.1186/s12933-015-0268-2
23. Liu W, Yang C, Lei F, et al. Major lipids and lipoprotein levels and risk of blood pressure elevation: a Mendelian Randomisation study. EBioMedicine. 2024;100:104964. DOI:10.1016/j.ebiom.2023.104964
24. Suliman ME, Qureshi AR, Troise D, et al. Plasma branched-chain amino acids in chronic kidney disease: associations with atherogenic lipids and mortality. Amino Acids. 2026 Mar 8;58(1):20. DOI:10.1007/s00726-026-03511-7
25. Suh SH, Oh TR, Choi HS, et al. Serum triglycerides level is independently associated with renal outcomes in patients with non-dialysis chronic kidney disease: Results from KNOW-CKD study. Front Nutr. 2022 Nov 24;9:1037618. DOI:10.3389/fnut.2022.1037618
26. Rizk JG, Hsiung JT, Arif Y, et al. Triglycerides and Renal Outcomes According to Albuminuria and in Consideration of Other Metabolic Syndrome Components in Diabetic US Veterans. Am J Nephrol. 2023;54(1-2):14-24. DOI:10.1159/000529414
27. Zhu B, Shi Y, Song N, et al. Associations between metabolic profiles and incident CKD in the Chinese population aged 45-85 years. Int Urol Nephrol. 2024; 56(7):2325-2336. DOI:10.1007/s11255-023-03916-3
28. Murkamilov IT, Fomin VV, Murkamilova Zh A, et al. Association of hypertriglyceridemia with risk factors for cardiovascular and renal complications in individuals with high cardiovascular risk. Russian Journal of Cardiology. 2023;28(2):42-49. Russian. DOI:10.15829/1560-4071-2023-5215
29. Murkamilova ZhA, Fomin VV, Sabirov IS, et al. Prevalence of risk factors of cardiovascular events and functional state of the kidneys with comorbidities in patients of different age groups. Russian Journal of Preventive Medicine. 2023;26(1):59-69. Russian. DOI:10.17116/profmed20232601159
30. Dolgalev IV, Brazovskaya NG, Ivanova AYu et al. Impact of hypertension, overweight, hypertriglyceridemia and their combination for mortality rate according to the results of a 27-year cohort prospective study. Cardiology. 2019;59(11S):44-52). Russian. DOI:10.18087/cardio.n344
31. Du X, Ding J, Ma X, et al. Remnant cholesterol has an important impact on increased carotid intimamedia thickness in nondiabetic individuals. Int. J. Cardiovasc. Imaging. 2023. DOI:10.1007/s10554023029570
32. Heo JH, Jo SH. Triglyceride-Rich Lipoproteins and Remnant Cholesterol in Cardiovascular Disease. J Korean Med Sci. 2023; 25;38(38):e295. DOI:10.3346/jkms.2023.38.e295
33. Assanto E, Brigato C, Gammaitoni G, et al. Assessment of Triglyceride/High-Density Lipoprotein Cholesterol Ratio and Triglyceride-Glucose Index Threshold in Patients with Chronic Kidney Disease: Evaluation of Clinical Features and Outcomes. High Blood Press Cardiovasc Prev. 2026 Mar;33(2):217-225. DOI:10.1007/s40292-025-00771-4
34. Tsygankova OV, Apartseva NE, Ametov AS. Hypertriglyceridemia—a new and important present. Endocrinology: News, Opinions, Training. 2023;12:4:99–111. Russian. DOI: 10.33029/2304-9529-2023 12-4-99-111
35. Murkamilov IT, Aitbaev KA, Fomin VV, et al. Non-high-density lipoprotein cholesterol (non-HDL-cholesterol) in chronic kidney disease: clinical and functional significance. Therapy.2026;12(1):42-53. Russian. DOI:10.18565/therapy.2026.1.42-53

36. Bhatt DL, Steg PG, Miller M et al.; REDUCE-IT Investigators. Cardiovascular Risk Reduction with Icosapent Ethyl for Hypertriglyceridemia. N Engl J Med. 2019;380(1):11–22. DOI:10.1056/NEJMoa1812792

37. Kanorskiy SG, Mamedov MN Correction of hypertriglyceridemia and ways to improve the prognosis of patients. International Journal of Heart and Vascular Diseases. 2024;12(42): 39-48. Russian. DOI:10.24412/2311-1623 2024-42-39-48

International Heart and Vascular Disease Journal. Volume 14, № 50, June 2026
ISSN: 2311-1623 (Print)
ISSN: 2311-1631 (Online)
http://www.heart-vdj.com

Association of salivary cortisol levels with cardiovascular diseases

Burmistrov M.E.[1], Burmistrova L.F.[1], Petrov M.V.[1], Komissarenko I.A.[2], Markov V.V.[1]

[1] Penza State University, Penza, Russia.
[2] Russian University of Medicine, Moscow, Russia.

AUTHORS

Maxim E. Burmistrov*, Resident Physician, Penza State University; Penza, Russia. ORCID: 0000-0001-9000-1565
Larisa F. Burmistrova, PhD, MD, Associate Professor, Penza State University, Penza, Russia. ORCID: 0000-0002-6568-0305
Mikhail V. Petrov, PhD, MD, Associate Professor, Penza State University, Penza, Russia. ORCID: 0000-0003-0542-4040
Irina A. Komissarenko, PhD, MD, Professor, Russian University of Medicine, Moscow, Russia. ORCID: 0000-0001-5621-2721
Vladimir V. Markov, PhD, MD, Associate Professor, Penza State University, Penza, Russia. ORCID: 0009-0002-5880-6966

Cardiovascular diseases continue to be the leading cause of mortality in developed countries, while traditional risk factors do not fully explain the variability in the development and progression of atherosclerosis. In recent decades, significant attention has been paid to the role of chronic psychosocial stress and hypercortisolemia as independent cardiovascular risk factors.

Aim. To evaluate the relationship between morning salivary cortisol concentration and dyslipidemia parameters, anthropometric measurements, and the severity of atherosclerotic lesions of the carotid and coronary arteries in patients with cardiovascular risk factors.

Material and methods. The study included 50 patients with cardiovascular risk factors. All participants underwent salivary cortisol level measurement, lipid profile assessment, and anthropometry. The severity of atherosclerosis was assessed by carotid intima-media thickness (IMT) and by the SYNTAX Score on coronary angiography.

Results. The mean salivary cortisol level was 8.4±3.2 nmol/L. Statistically significant correlations were found between cortisol level and triglyceride levels, total cholesterol, low-density lipoprotein cholesterol, body mass index, and waist circumference. The strongest associations were observed with markers of atherosclerosis: intima-media thickness and SYNTAX Score. Patients with cortisol levels above the median (>8.1 nmol/L) had significantly higher intima-media thickness values (1.14± 0.18 mm vs. 0.92±0.14 mm, p=0.003) and SYNTAX Score (22.5±8.4 vs. 11.3±6.7, p<0.001).

* Corresponding author. Tel. +7 (906) 397-9036; e-mail: . E-mail: lamax-69@mail.ru

Conclusion. Elevated salivary cortisol level, as a marker of chronic hypercortisolemia, is associated with more pronounced manifestations of dyslipidemia (hypertriglyceridemia, impaired lipoprotein ratio), abdominal obesity, and a greater extent of atherosclerotic lesions in major arteries. Salivary cortisol measurement may become a useful tool for cardiometabolic risk stratification.

Keywords: salivary cortisol, dyslipidemia, abdominal obesity, intima-media thickness, SYNTAX Score, atherosclerosis.

Conflict of Interest: none declared.

Received: 27.02.2026
Accepted: 10.05.2026

For citation: Burmistrov ME, Burmistrova LF, Petrov MV et al. Association of Salivary Cortisol Levels with Cardiovascular Diseases. International Heart and Vascular Diseases Journal. 2026; 14(50): 27-33. DOI: 10.24412/2311-1623-2026-50-32-39

Introduction

Cardiovascular diseases (CVD) associated with atherosclerosis continue to be the leading cause of mortality in developed countries. Traditional risk factors (RF) (dyslipidemia, arterial hypertension (AH), smoking, diabetes mellitus) do not fully explain the variability in the development and progression of atherosclerosis. In recent decades, considerable attention has been paid to the role of chronic psychosocial stress as an independent cardiovascular risk factor [1].

A key mediator of the adaptive response to stress is cortisol, the primary glucocorticoid hormone in humans. Prolonged or excessive activation of the hypothalamic-pituitary-adrenal (HPA) axis, leading to chronic hypercortisolemia, exerts a systemic negative impact on metabolism. Cortisol stimulates lipolysis in the extremities and lipogenesis in the abdominal region, contributing to the development of visceral obesity, induces insulin resistance, impairs endothelial function, enhances pro-inflammatory processes and oxidative stress, collectively creating a pro-atherogenic environment [2].

Traditionally, cortisol is measured in serum or 24-hour urine; however, these methods have limitations (invasiveness of collection, influence of circadian rhythm, stress from venipuncture). Determination of free (biologically active) cortisol in saliva is a non-invasive, convenient, and valid method, correlating well with the level of free cortisol in plasma. Salivary cortisol reflects the short-term activity of the HPA axis and is widely used in studies linking stress and somatic pathology [3].

Despite the existence of theoretical premises, there are insufficient comprehensive studies examining the relationship between salivary cortisol levels and objective markers of atherosclerosis in different vascular beds (carotid and coronary arteries) within the same group of patients. Most studies focus either on the lipid profile or on individual ultrasound parameters.

Aim of the study. To evaluate the relationship between morning salivary cortisol concentration and dyslipidemia parameters, anthropometric measurements, and the severity of atherosclerotic involvement of the carotid and coronary arteries in patients with cardiovascular risk factors.

Material and methods

A single-center, cross-sectional, observational study was conducted. The study included 50 patients (32 men and 18 women) aged 42 to 77 years (mean age—58.3±8.7 years), who were undergoing examination and treatment in the cardiology departments of the Zakharin Clinical Hospital No. 6 in Penza with suspected coronary artery disease (CAD) or for cardiovascular risk assessment. Inclusion criteria: age from 40 to 80 years; presence of at least two classic CVD risk factors (AH, dyslipidemia, smoking, positive family history, obesity); written informed consent to participate. Exclusion criteria: acute coronary syndrome or stroke within the preceding 3 months; severe endocrine diseases (Cushing's syndrome, Addison's disease); oncological pathology; severe hepatic or renal failure; acute infectious diseases; use of systemic glucocorticoids or drugs significantly affecting lipid metabolism (statins could be discontinued by agreement with the attending physician for 2 weeks before blood sampling at the start of the study).

All patients underwent the following examinations:

Medical history and anthropometry: Age, sex, and diagnoses were recorded. Height, weight, and waist circumference (WC) were measured. Body mass index (BMI) was calculated using the formula:

$$\text{weight (kg)} / \text{height}^2 \text{ (m}^2\text{)}.$$

Abdominal obesity (AO) was diagnosed with WC ⩾ 94 cm for men and ⩾80 cm for women.

Determination of salivary cortisol: Saliva samples were collected in the morning (from 8:00 to 9:00 AM) on an empty stomach, at rest, at least 1 hour after waking. Patients refrained from smoking, eating, and brushing teeth for 1 hour before collection. Sterile saliva collection tubes were used. Samples were centrifuged and stored at –80 °C until analysis. Cortisol concentration was determined by enzyme-linked immunosorbent assay using a reagent kit for cortisol determination (JSC "BioKhimMak", Russia). Sensitivity of the method—0.5 nmol/L. Intra- and inter-assay coefficients of variation did not exceed 8%.

Biochemical blood test: Venous blood was drawn in the morning on an empty stomach. The following were determined: total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) (calculated by the Friedewald formula), and triglycerides (TG) using an enzymatic colorimetric method. The atherogenic index (LDL-C/HDL-C) was calculated.

Assessment of carotid atherosclerosis: Ultrasound examination of the carotid arteries was performed using a Vivid S6 diagnostic ultrasound system (General Electric, Israel). Intima-media thickness (IMT) was measured in the distal segments of the common carotid arteries, bifurcations, and proximal segments of the internal carotid arteries according to standard methodology. The averaged IMT value (mean value across 12 segments) was used for analysis. The presence of atherosclerotic plaques (localized wall thickening >1.5 mm or 0.5 mm greater than adjacent segments) was recorded.

Assessment of coronary atherosclerosis: All patients underwent coronary angiography based on clinical indications (stable angina class III-IV, positive stress tests). The presence of hemodynamically significant stenoses (>50% diameter) in the major epicardial arteries was assessed. A dichotomous variable was used for analysis: presence/absence of ⩾1 significant stenosis. The anatomical complexity of coronary atherosclerosis in all patients was quantitatively assessed using the angiographic SYNTAX Score (SS). The score was calculated based on selective coronary angiography data according to the official algorithm. All hemodynamically significant lesions (stenosis ⩾50% in vessels with diameter ⩾1.5 mm) were assessed, taking into account their location, morphological complexity (occlusion, bifurcation/trifurcation, length, calcification, thrombus, etc.), and the type of coronary circulation. The final score represents the sum of the scores for all lesions. Depending on the SS value, patients were stratified into groups of low (SS⩽22), intermediate (SS 23–32), and high (SS⩾33) risk.

Ethical review

The study was conducted in accordance with Good Clinical Practice standards and the principles of the Declaration of Helsinki. The study protocol was approved by the Local Ethics Committee of Penza State University (Protocol No. 9 dated May 31, 2024). All participants signed informed consent.

Statistical analysis

Statistical processing was performed using the Statistica 10.0 (Stat Soft Inc., USA) and SPSS Statistics 23.0 (IBM, USA) software packages. The normality of the distribution of quantitative variables was checked using the Shapiro-Wilk test. Normally distributed data are presented as M±SD, non-normally distributed as Me [Q1; Q3]. Student's t-test or the non-parametric Mann-Whitney U-test was used to compare two independent groups. Qualitative variables were described using absolute values and percentages. Qualitative variables were compared using the Pearson chi-square (χ^2) test. Pearson's (r) or Spearman's (rs) correlation coefficients were used to assess correlations. Sensitivity and specificity analysis of the predictive role of cortisol was performed using receiver operating characteristic (ROC) curves. The overall accuracy of the method is presented as the area under the ROC curve (AUC). Differences were considered statistically significant at $p < 0.05$.

Results of the study

The mean age of patients was 58.3±8.7 years. The sex distribution was as follows: 64% men (n=32) and 36% women (n=18). The mean values of the main studied parameters are presented in Table 1. AO was diagnosed in 36 patients (72%). Elevated TG levels (>1.7 mmol/L) were observed in 29 patients (58%), and low HDL-C levels (<1.0 mmol/L for men, < 1.2 mmol/L for women) were observed in 21 patients (42%). The mean salivary cortisol level was 8.4±3.2 nmol/L (range 3.1 to 16.8 nmol/L), with a median value of 8.1 nmol/L. Increased IMT (⩾0.9 mm)

DOI: 10.24412/2311-1623-2026-50-32-39

Table 1. **General characteristics of the examined patients**

Parameter	All patients, (n=50)	Men, (n=32)	Women, (n=18)	p 2-3
	1	2	3	
Age, years	58.3 ± 8.7	56.9 ± 9.1	60.8 ± 7.5	0.121
BMI, kg/m²	30.1 ± 4.5	29.5 ± 4.0	31.2 ± 5.1	0.185
WC, cm	101.8 ± 11.3	102.5 ± 10.8	100.5 ± 12.4	0.543
Salivary cortisol, nmol/L	8.4 ± 3.2	8.6 ± 3.4	8.0 ± 2.8	0.512
TC, mmol/L	5.6 ± 1.1	5.4 ± 1.0	5.9 ± 1.2	0.098
LDL-C, mmol/L	3.5 ± 0.9	3.4 ± 0.8	3.7 ± 1.1	0.245
HDL-C, mmol/L	1.2 ± 0.3	1.1 ± 0.3	1.3 ± 0.3	0.019
TG, mmol/L	2.0 [1.5; 2.7]	2.1 [1.6; 2.8]	1.8 [1.4; 2.4]	0.210
Atherogenic index (LDL-C/HDL-C)	3.0 [2.4; 3.8]	3.1 [2.6; 3.9]	2.8 [2.1; 3.3]	0.087
Mean IMT, mm	1.03 ± 0.20	1.05 ± 0.21	0.99 ± 0.18	0.308
Presence of atherosclerotic plaques, n (%)	34 (68%)	23 (72%)	11 (61%)	0.430
SYNTAX Score	16.4 [8.0; 25.0]	17.6 [9.0; 26.0]	15.6 [6.0;23.0]	0.045

Note. Data are presented as M±SD or Me [Q1; Q3], p—significance level of differences between men and women (t-test or Mann-Whitney U-test). The χ^2 test was used to compare categorical variables (presence of plaques). Statistically significant differences were obtained for HDL-C and the degree of coronary artery involvement (SYNTAX Score).

and/or presence of plaques in the carotid arteries were detected in 33 patients (66%). The SYNTAX Score was 16.4 [8.0; 25.0].

Subsequently, a correlation analysis was performed, the results of which demonstrated the presence of statistically significant positive relationships between salivary cortisol levels (a marker of chronic stress and HPA axis activity) and most of the studied cardiometabolic parameters (Table 2).

When analyzing salivary cortisol levels and the lipid spectrum, statistically significant moderate positive correlations were found with TC, LDL-C, and TG. The correlation with HDL-C was negative but did not reach statistical significance. Significant moderate positive correlations were identified. This confirms the known role of cortisol in the pathogenesis of abdominal (visceral) obesity—the most metabolically dangerous type of obesity. Among all parameters, the most significant moderate positive correlation was with carotid artery IMT. IMT is an ultrasound marker of early atherosclerosis and subclinical vascular damage. Such a close relationship indicates a direct association between the level of chronic stress (cortisol) and structural changes in the arteries. A strong positive correlation was also found with the SYNTAX Score, which quantitatively assesses the anatomical complexity and extent of coronary artery involvement. The moderate correlation with cortisol suggests that chronic stress may be associated not only with early but also with pronounced, clinically significant forms of CAD.

A comparative analysis of patient groups with low and high salivary cortisol levels was also conducted. When the sample was divided by the median cortisol value (8.1 nmol/L), significant differences were identified (Table 3). The high cortisol group (>8.1 nmol/L, n=29) had significantly higher values of WC, TG, atherogenic index, IMT, and coronary atherosclerosis compared to the low cortisol group (≤8.1 nmol/L,

Table 2. **Correlation of salivary cortisol levels with the studied parameters**

Parameter	Correlation coefficient (r/rs)	p
TC	0.45	0.007
TC LDL-C	0.51	<0.001
TC HDL-C	0.22	0.127
TG	0.39	0.009
BMI	0.32	0.004
WC	0.41	0.008
Carotid artery IMT	0.61	<0.001
SYNTAX Score	0.58	<0.001

Note. r/r_s—Pearson's or Spearman's correlation coefficient; p—level of statistical significance. Statistically significant correlations ($p < 0.05$) are highlighted.

Table 3. **Comparison of groups with low and high salivary cortisol levels**

Parameter	Group 1: cortisol ≤ 8.1 nmol/L (n=29)	Group 2: cortisol > 8.1 nmol/L (n=21)	p
Cortisol, nmol/l	5.9 ± 1.6	11.0 ± 2.1	<0.001
WC, cm	95.2 ± 9.1	108.4 ± 10.0	<0.001
TG, mmol/l	1.6 [1.3; 2.0]	2.5 [1.9; 3.2]	<0.001
LDL-C/HDL-C	2.6 [2.1; 3.2]	3.5 [2.9; 4.2]	0.001
Mean IMT, mm	0.92 ± 0.14	1.14 ± 0.18	0.003
Hemodynamically significant coronary artery stenoses	9.8 ± 3.0	6.9 ± 2.8	0.011

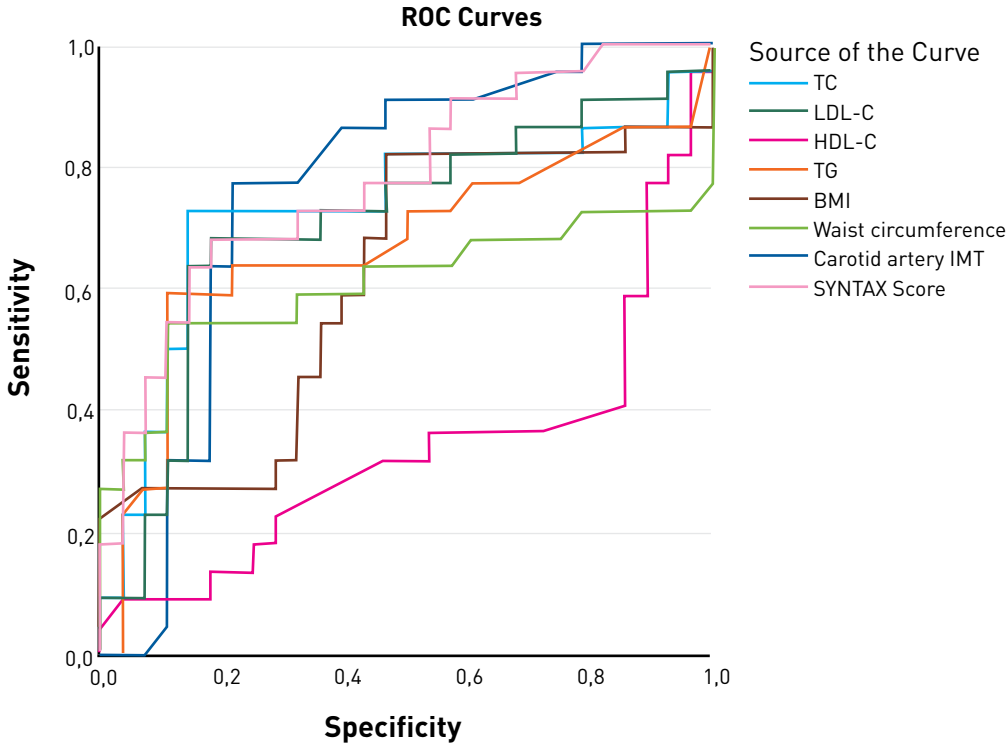

Fig. 1. ROC curve of the predictive role of salivary cortisol in the assessment of the studied parameters
*__Note.__ Area under the ROC curve (AUC): TC = 0.729; LDL-C = 0.705; HDL-C = 0.335; TG = 0.671; BMI = 0.614; WC = 0.608; carotid artery IMT = 0.761; SYNTAX Score = 0.780.

n=21). No differences in age, sex, BMI, or TC were observed between the groups.

Among the 50 patients who underwent coronary angiography, hemodynamically significant stenoses were detected in 29 individuals (57%). All patients with high salivary cortisol levels had plaques in the carotid arteries upon ultrasound examination.

At the final stage, an ROC analysis of the predictive role of salivary cortisol in assessing the studied parameters (TC, LDL-C, HDL-C, TG, BMI, WC, carotid artery IMT, SYNTAX Score) was performed (Fig. 1).

Discussion

The conducted study allowed us to identify a significant prevalence of cardiovascular risk factors and subclinical atherosclerosis among the examined middle-aged patients with CAD. The main result of the study is the demonstration of significant associations between salivary cortisol levels, which is an integrative marker of HPA axis activity and chronic psychosocial stress, and key parameters of lipid metabolism, AO, as well as the severity of atherosclerotic involvement of the carotid and coronary arteries.

The examined patient group was characterized by a high frequency of AO (72%) and atherogenic dyslipidemia (elevated TG—58%, low HDL-C—42%), which corresponds to current concepts of metabolic syndrome as a crucial pathogenetic link in CVD [4]. he mean salivary cortisol level (8.4±3.2 nmol/L) was within the physiological range, which is expected for patients without endocrine pathology and confirms that the observed associations are mediated by prolonged, rather than acute, glucocorticoid exposure.

The correlation analysis data are consistent with the known pathophysiological effects of cortisol. Moderate positive correlations with TC (r=0.45), LDL-C (r=0.51), and TG (r=0.39) reflect the stimulating effect of chronic hypercortisolemia on the synthesis of very low-density lipoproteins in the liver, activation of lipolysis in visceral adipose tissue with subsequent increased flow of free fatty acids into the portal circulation, and the development of insulin resistance [2, 5]. The trend towards a negative correlation with HDL-C, which did not reach statistical significance in our sample, is also described in the literature and may be related to decreased lipoprotein lipase activity [6]. The identified correlations between cortisol levels and BMI (r=0.32) and, especially, with WC (r=0.41) confirm the central role of the HPA axis in the pathogenesis of abdominal (visceral) obesity, which is a key

component of metabolic syndrome and an independent risk factor for cardiovascular events [7].

The most significant results are the moderate positive correlations between salivary cortisol levels and the ultrasound marker of subclinical atherosclerosis—carotid artery IMT (r=0.61), as well as with the quantitative indicator of coronary bed involvement—the SYNTAX Score (r=0.58). These data suggest that cortisol-mediated chronic stress is associated not only with metabolic disorders but also directly with structural and functional changes in blood vessels. The results are consistent with studies demonstrating a link between elevated cortisol levels (including salivary), arterial stiffness, and endothelial dysfunction [8]. Proposed mechanisms include the direct pro-atherogenic effect of glucocorticoids on the vascular wall, enhancement of oxidative stress, pro-inflammatory processes, and smooth muscle cell proliferation [9].

Additional confirmation of the clinical significance of the identified relationships comes from the results of the comparative analysis of groups divided by the median cortisol level. Patients with cortisol concentration >8.1 nmol/L had significantly higher values of WC, TG, atherogenic index (LDL-C/HDL-C), IMT, and more severe coronary artery involvement, despite comparable age, sex, and BMI. This fact emphasizes that even within the framework of physiological fluctuations, a relatively higher basal cortisol level can act as a marker of an unfavorable cardiometabolic and atherosclerotic profile [10, 11]. It is important to note that all patients in the high cortisol subgroup were found to have atherosclerotic plaques in the carotid arteries.

The results of the ROC analysis indicate a significant predictive role of salivary cortisol levels in assessing the risk of cardiometabolic disorders and the degree of atherosclerotic involvement [10]. The highest diagnostic accuracy, determined by AUC, was noted for indicators of coronary atherosclerosis severity and structural vascular changes: SYNTAX Score (AUC=0.780), carotid artery IMT (AUC=0.761), as well as for TC=0.729 and LDL-C=0.705, which is consistent with data on the pathogenetic link between chronic stress and dyslipidemia [6, 7].

Limitations of the conducted study: the cross-sectional and single-center nature of the study, which included a small sample size (n=50). The study included patients with already suspected or diagnosed CAD. A single measurement of salivary cortisol (morning) was performed, which has high variability and may not fully reflect chronic HPA axis activity.

Ways to overcome limitations: conducting a prospective multicenter study involving a larger number of participants to increase power and representativeness. Inclusion of not only cardiology patients but also individuals from the general population with different levels of cardiovascular risk, including healthy volunteers. Determination of cortisol in several saliva samples throughout the day to calculate its daily variability.

The obtained data allow considering salivary cortisol determination as a promising non-invasive biomarker for the integrated assessment of cardiovascular risk.

Conclusion

In patients with CVD risk factors, elevated morning salivary cortisol levels were associated with more pronounced manifestations of metabolic syndrome: abdominal obesity (by waist circumference), hypertriglyceridemia, and an increased atherogenic index.

An independent positive association was found between salivary cortisol concentration and objective markers of vascular atherosclerotic involvement: carotid artery IMT and coronary calcium index.

Patients with hemodynamically significant coronary artery stenoses according to angiography had significantly higher salivary cortisol levels compared to patients without significant stenoses.

Determination of salivary cortisol can be considered as an additional, non-invasive tool for the stratification of cardiometabolic risk, integrating the impact of chronic stress on metabolism and the vascular wall.

Conflict of Interest: none declared.

References

1. Manolis TA, Manolis AA, Manolis AS. Emotional stress in cardiac and vascular diseases. Curr Vasc Pharmacol. 2025;23(3):172-195. DOI: 10.2174/0115701611328094241104062903
2. Mohd Azmi NAS, Juliana N, Azmani S et al. Cortisol on circadian rhythm and its effect on cardiovascular system. Int J Environ Res Public Health. 2021; 14;18(2):676. DOI: 10.3390/ijerph18020676

3. Khawagi WY, Al-Kuraishy HM, Hussein NR, et al. Depression and type 2 diabetes: A causal relationship and mechanistic pathway. Diabetes Obes Metab. 2024;26(8):3031-3044. DOI: 10.1111/dom.15630
4. Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2019; 25;73(24):e285-e350. DOI: 10.1016/j.jacc.2018.11.003
5. Grabner GF, Xie H, Schweiger M, Zechner R. Lipolysis: cellular mechanisms for lipid mobilization from fat stores. Nat Metab. 2021;3(11):1445-1465. DOI: 10.1038/s42255-021-00493-6
6. Schowe AM, Czamara D, Lahti-Pulkkinen M, et al. Serial diurnal salivary cortisol profiles in 667 pregnant women-association with cardiometabolic complications. J Clin Endocrinol Metab. 2024;109(10):2491-2503. DOI:10.1210/clinem/dgae202
7. Dollet L, Zierath JR. Interplay between diet, exercise and the molecular circadian clock in orchestrating metabolic adaptations of adipose tissue. J Physiol. 2019; 597(6):1439-1450. DOI: 10.1113/JP276488
8. von Haehling S, Foldes G, Papp Z, Anker SD. Creating an impact, not an impression: ESC Heart Failure in its seventh year. ESC Heart Fail. 2021;8(5):3451-3452. DOI: 10.1002/ehf2.13636
9. Liu MY, Wei LL, Zhu XH et al. Prenatal stress modulates HPA axis homeostasis of offspring through dentate TERT independently of glucocorticoids receptor. Mol Psychiatry. 2023; 28(3):1383-1395. DOI: 10.1038/s41380-022-01898-9
10. Feng X, Jia M, Cai M et al. Central-peripheral neuroimmune dynamics in psychological stress and depression: insights from current research. Mol Psychiatry. 2025;30(10):4881-4898. DOI: 10.1038/s41380-025-03085-y
11. Sandrini L, Ieraci A, Amadio P et al. Impact of Acute and Chronic Stress on Thrombosis in Healthy Individuals and Cardiovascular Disease Patients. Int J Mol Sci. 2020; 22;21(21):7818. DOI: 10.3390/ijms21217818

DOI:10.24412/2311-1623-2026-50-40-47

Remote monitoring in elderly patients with chronic heart failure after pacemaker implantation

Peshkov S.A.[1], Povarov V.O.[1,2]

[1] Regional Clinical Cardiology Dispensary, Ryazan, Russia.
[2] Ryazan State Medical University named after Academician I.P. Pavlov, Ryazan, Russia.

AUTHORS:

Sergey A. Peshkov*, Cardiologist, Department of Cardiologist, Department of Surgical Treatment of Complex Cardiac Arrhythmias and Electrocardiostimulation, Ryazan Regional Clinical Cardiology Dispensary, Ryazan, Russia. ORCID: 0009-0002-9225-3533

Vladislav O. Povarov, PhD, MD, Head of the Head, Department of Surgical Treatment of Complex Cardiac Rhythm Disorders and Electrocardiostimulation, Ryazan Regional Clinical Cardiological Dispensary, Ryazan, Russia; Associate Professor of the Department of Cardiovascular Surgery, X-ray Endovascular Surgery and Radiation Diagnostics, I.P. Pavlov Ryazan State Medical University, Ryazan State Medical University named after Academician I.P. Pavlov, Ryazan, Russia. ORCID: 0000-0001-8810-9518

Aim. To evaluate the impact of remote telemetry monitoring on the course of chronic heart failure (CHF), functional status, and quality of life (QoL) in patients over 60 years of age after dual-chamber pacemaker (PM) implantation.

Material and methods. This prospective study included 95 patients (49.5% male), mean age 72.5±7.9 years. The main group of patients (n=40) was remotely monitored using the CareLink Network remote monitoring system (Medtronic, USA). Data transmission was performed monthly for one year. The control group (n=55) underwent in-person clinical follow-up at 1 month and 1 year after surgery. The study and control groups were comparable in age, sex, nosological forms, clinical and demographic characteristics, and indications for surgery ($p>0.05$). CHF course was assessed using clinical and instrumental parameters, and QoL was assessed using the Minnesota Living with Heart Failure Questionnaire (MLHFQ).

Results. The study found no difference in hospitalization rates based on the follow-up method ($p>0.05$). A significant improvement in the clinical status score was observed in the entire cohort ($p<0.001$). The 6-minute walk test distance significantly increased in the remote monitoring group ($p=0.011$) compared to the control group ($p=0.229$). Quality of life according to the MLHFQ significantly improved in both groups one year after surgery ($p<0.001$). However, the reduction in the total score and

* Corresponding author. Tel. +7 910-568-3076. E-mail: sergeypeshkov87@yandex.ru

the subscales "Economic aspects" and "Emotional aspects" was significantly greater in the remote monitoring group (p=0.002; p=0.014; p<0.001, respectively).
Conclusion. In patients over 60 years of age with CHF, pacemaker implantation leads to a significant improvement in clinical status, functional status, and quality of life, regardless of the subsequent follow-up method. At the same time, a significant increase in the 6-minute walk test distance after one year was achieved only with the use of remote monitoring, indicating its advantage in improving exercise tolerance. Comparable hospitalization rates and no changes in echocardiographic parameters in both groups confirm the efficacy and safety of remote follow-up.

Keywords: heart failure, pacemaker, quality of life, remote monitoring.

Conflict of interest: none declared.

Received: 25.03.2026
Accepted: 05.03.2026

For citation: Peshkov S.A., Povarov V.O. Remote monitoring in elderly patients with chronic heart failure after pacemaker implantation. International Heart and Vascular Disease Journal. 2026;14(50):34-40. DOI: 10.24412/2311-1623-2026-50-40-47

Introduction

Chronic heart failure (CHF), despite recent advances in pharmacological treatment, retains its status as a serious disease requiring constant dynamic monitoring and control. An effective mechanism for improving the accessibility of care for patients with CHF, ensuring rapid response to changes in condition, and enhancing treatment adherence is remote monitoring (RM) [1]. Modern cardiology employs a wide range of RM technologies, from comprehensive telephone support to complex implantable systems that transmit physiological data [2–4].

It is known that long-term right ventricular pacing negatively affects left ventricular function, contributing to the development of heart failure, especially in patients with concomitant cardiovascular diseases [5, 6], and worsens the prognosis. Implantation of a biventricular pacemaker (PPM), by addressing dyssynchrony, improves the pumping function of the heart [7].

However, the effectiveness of RM in improving clinically significant outcomes in patients with CHF remains a subject of debate, and data from randomized clinical trials are conflicting [8, 9]. For example, a meta-analysis by Ezimoha et al., summarizing the results of 15 studies, did not reveal a statistically significant effect of RM on mortality but demonstrated a reduction in heart failure-related hospitalizations [8]. At the same time, a review by Calvanese et al. showed that modern multiparametric telemonitoring algorithms integrated with implantable devices can improve clinical outcomes in patients with implantable cardioverter-defibrillators (ICDs) and cardiac resynchronization therapy (CRT) devices through early detection of decompensation [9]. Such variability in results may be related to differences in study design, monitoring frequency, technologies used, and patient populations [1].

Current research focuses on analyzing the performance of complex implanted devices (ICD/CRT) in patients with severe systolic dysfunction [10, 11]. At the same time, the value of simpler and more accessible forms of RM (e.g., based on regular interviews and transmission of basic parameters) for patients after implantation of standard dual-chamber pacemakers, who also constitute a large group at risk for the development and progression of CHF, especially in the elderly, remains significantly less studied.

Aim of the study. To evaluate the impact of remote telemetric monitoring on the course of CHF, functional status, and quality of life in patients over 60 years of age after implantation of dual-chamber pacemakers

Material and methods

This work is a prospective single-center study involving 95 patients of both sexes after primary implantation of a dual-chamber pacemaker at the Department of Surgical Treatment of Complex Cardiac Arrhythmias and Electrocardiostimulation.

The study included patients over 60 years of age with second- or third-degree atrioventricular blocks or sick sinus syndrome.

The main and control groups were comparable in age, sex, nosological forms, clinical and demographic characteristics, indications for surgery (Table 1), as well as in all groups of medications taken (angio-

DOI:10.24412/2311-1623-2026-50-40-47

Table 1. **Clinical and demographic characteristics of patients included in the study**

Parameter	Study group (n=40)	Control group (n=55)	p
Age, years, M±SD	73.20±6.89	72.02±8.53	0.472
Sex, n (%) Male Female	 18 (45.0 %) 22 (55.0 %)	 29 (52.7 %) 26 (47.3 %)	0.457
Body mass index, kg/m², Me [Q1; Q3]	28.06 [25.77; 30.84]	27.04 [24.33; 29.91]	0.187
Body surface area, m², Me [Q1; Q3]	1.95 [1.83; 2.06]	1.96 [1.85; 2.00]	0.818
Underlying disease, n (%)		0.267	0.267
—Atrioventricular block, n (%)	24 (60.0 %)	39 (70.9 %)	
—Sick sinus syndrome, n (%)	16 (40.0 %)	16 (29.1 %)	
Comorbidities, n (%)			
Coronary artery disease, n (%)	39 (97.5 %)	53 (96.4 %)	1
Hypertension, n (%)	40 (100.0 %)	52 (94.5 %)	0.261
Angina pectoris, n (%)	4 (10.0 %)	11 (20.0 %)	0.257
Myocardial infarction (MI) in history, n (%)	6 (15.0 %)	10 (18.2 %)	0.785
CHF, n (%)			
Functional class (FC) 1	2 (5.0%)	9 (16.4 %)	0.218
FC 2	14 (35.0 %)	20 (36.4 %)	
FC 3	23 (57.5 %)	26 (47.3 %)	
FC 4	0 (0 %)	0 (0 %)	
Stroke in history, n (%)	3 (7.5 %)	2 (3.6 %)	0.647
Diabetes mellitus, n (%)	11 (27.5 %)	9 (16.4 %)	0.189

Note. [Q1; Q3]—interquartile range; p—significance level; SD—standard deviation.

tensin-converting enzyme inhibitors, sartans, beta-blockers, mineralocorticoid receptor antagonists, sodium-glucose cotransporter 2 inhibitors, diuretics) (p>0.05).

The first group of patients (n=40) constituted the main group. Patients in this group were given a monitor for remote data transmission "CareLink Network" (Medtronic, USA) and were instructed on how to use it. The transmitted information included: periodic intracardiac electrogram data, number and type of detected arrhythmias, percentage of atrial and ventricular pacing, estimated battery life of the pacemaker, and pacing thresholds for both channels.

Patients in the control group (n=55) were followed up in person at the clinic one month after implantation and then again after one year.

The dynamics of CHF were assessed before surgery and after 1 year based on the Clinical Status Assessment Scale (CSAS) for CHF patients, the 6-minute walk test (6MWT), and echocardiography (EchoCG) data. Quality of life (QoL) was assessed using the Minnesota Living with Heart Failure Questionnaire (MLHFQ) before surgery, at 5 days, 1 month, and 1 year after surgery. The number of hospitalizations related to CHF and other causes was evaluated.

The research was approved by the Local Ethics Committee (Protocol No. 9 dated March 11, 2024). All patients participating in the study confirmed their consent by signing an informed consent form.

Statistical analysis

Statistical analysis was performed using StatTech v. 4.10.4 (developer: Stattech LLC, Russia). Data were described using the median (Me) and lower and upper quartiles (Q1–Q3). Comparison of two groups for a quantitative variable whose distribution differed from normal was performed using the Mann–Whitney U-test. Differences were considered statistically significant at p<0.05.

Results

Data obtained during the 12-month follow-up showed no deaths in the study. When analyzing other cardiovascular endpoints depending on the group, the frequency of hospitalizations was comparable (Table 2). There was no statistically significant difference in the causes of hospitalization (Table 3).

In the study group, there were 5 patients with two or more hospitalizations. The first patient had two hospitalizations related to paroxysmal supraventricular tachycardia (on days 122 and 181). The second had a hospitalization for hypertension on day 30 and for supraventricular tachycardia on day 210. The third had two hospitalizations with a diagnosis of enceph-

Table 2. **Number of hospitalizations depending on the group**

Parameter	Categories	Group		p
		Study group	Control group	
Hospitalization, n (%)	Yes	11 (27,5 %)	13 (23,6 %)	0,669
	No	29 (72,5 %)	42 (76,4 %)	

Note. p—significance level.

Table 3. **Causes of hospitalization depending on the group**

Parameters	Categories	Group		p
		Study group	Control group	
Stroke, n (%)	No	39 (97,5 %)	52 (94,5 %)	0,636
	Yes	1 (2,5 %)	3 (5,5 %)	
MI, n (%)	No	40 (100,0 %)	54 (98,2 %)	1,000
	Yes	0 (0,0 %)	1 (1,8 %)	
ACS, n (%)	No	36 (90,0 %)	51 (92,7 %)	0,717
	Yes	4 (10,0 %)	4 (7,3 %)	
CHF decompensation, n (%)	No	39 (97,5 %)	52 (94,5 %)	0,636
	Yes	1 (2,5 %)	3 (5,5 %)	

Note. p—significance level.

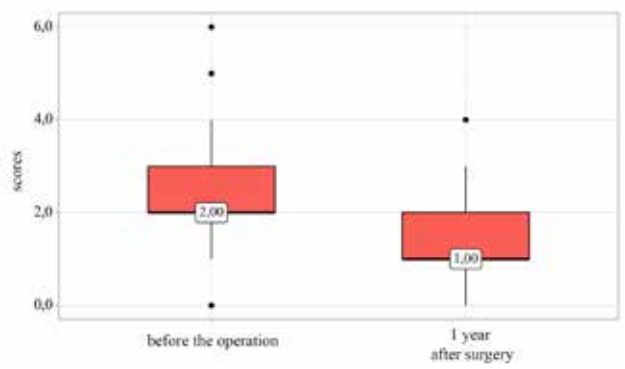

Fig. 1. Analysis of the dynamics of CSAS scores among all patients in the study

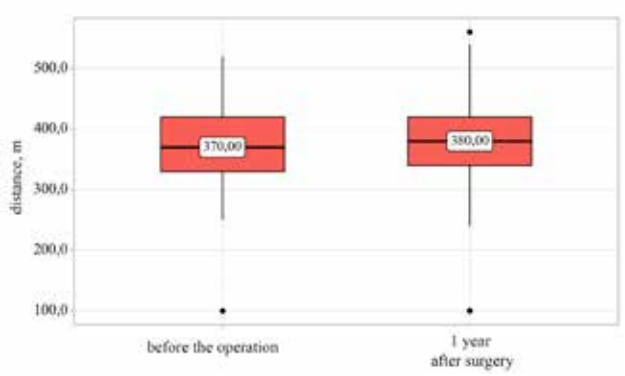

Fig. 2. Analysis of the dynamics of 6MWT results among all patients in the study

alopathy (days 178 and 365). The fourth had a hospitalization for acute coronary syndrome (ACS) on day 146 and for acute cerebrovascular accident (ACVA) on day 268. The fifth had a hospitalization in the rehabilitation department on day 60 and a hospitalization for ACVA on day 302.

In the control group, there were 3 such patients. The first patient—hospitalization for ACS on day 267 and for a newly diagnosed atrial fibrillation on day 370. The second patient—hospitalizations for CHF on day 32 and for ACS on day 360. The third patient—three hospitalizations in the rehabilitation department (on days 60, 120, and 360).

When analyzing the relationship between QoL according to the MLHFQ and the presence of repeated hospitalizations, we failed to identify statistically significant indicators either in the overall patient sample or in the control group (p>0.05).

At the same time, in the remote monitoring group, a significant association was found between an increased risk of rehospitalization and lower (worse) QoL scores: for the total score—at all follow-up time points (5 days, 1 month, and 1 year after surgery); "Economic Aspects"—at 5 days and 1 month; "Emotional Aspects"—at 1 month and 1 year after surgery.

When analyzing the dynamics of CSAS scores in all patients, a statistically significant improvement was revealed between the pre-operative stage (2.0 [2.0–3.0]) and 1 year later (1.0 [1.0–2.0]) (p<0.001). The results are presented in Figure 1.

The analysis showed that in all patients, regardless of the presence of rehospitalizations, there was a statistically significant improvement in clinical status (p<0.001). Similar data were obtained when dividing into the study and control groups (p<0.05).

When analyzing the dynamics of CSAS scores in the study and control groups, similar results were obtained: a statistically significant improvement was found between the pre-operative stage (2.0 [2.0–3.0]) and 1 year later (1.0 [1.0–2.0]) (p<0.001).

When analyzing the dynamics of 6MWT results, a statistically significant improvement was found between the pre-operative stage (370.0 [330.0–420.0]) and 1 year later (380.0 [340.0–420.0]) (p=0.007) among all patients in the study. The results are presented in Figure 2.

In the study group, when analyzing the dynamics of 6MWT results, a statistically significant improvement was found between the pre-operative

DOI:10.24412/2311-1623-2026-50-40-47

Table 4. **Echocardiography parameters over time before surgery and 1 year after surgery**

Parameter, Me [Q1; Q3]	Before surgery	1 year after	p
LA diameter, cm	4.1 (3.9–4.5)	4.1 (3.9–4.5)	0.423
RA diameter, cm	3.9 (3.7–4.2)	4.0 (3.7–4.4)	0.122
LV EDD, cm	5.4 (5.0–5.5)	5.3 (5.0–5.5)	0.56
LV ESD, cm	3.5 (3.2–3.6)	3.5 (3.2–3.7)	0.58
RV diameter, cm	2.6 (2.4–2.8)	2.6 (2.5–2.8)	0.079
LVEF, %	62.00 (60.00–65.00)	61.00 (60.00–64.00)	0.443
Mitral valve regurgitation, grade	2.0 (1.0–2.0)	2.0 (1.0–2.0)	0.694
Tricuspid valve regurgitation, grade	2.0 (1.0–2.0)	2.0 (1.0–2.0)	0.989
Aortic valve regurgitation, grade	1.0 (0.0–1.0)	1.0 (0.0–1.0)	0.827

Note. [Q1; Q3]—interquartile range; p—significance level.

Table 5. **Changes in quality of life according to the Minnesota Living with Heart Failure Questionnaire over 1 year of follow-up**

Parameter	Group	V0-V1	V0-V2	V0-V3
Total score	Study group	-4.00 [-5.00; -2.00]	-4.00 [-6.00; -2.00]	-9.00 [-14.00; -6.00]
	Control group	-3.00 [-6.50; -1.00]	-5.00 [-9.50; -2.00]	-4.00 [-10.50; 1.00]
	p	0.900	0.338	0.002
Economic aspects	Study group	-1.00 [-2.00; -1.00]	-1.50 [-3.00; -1.00]	-3.00 [-5.00; -2.00]
	Control group	-1.00 [-3.00; 0.00]	-2.00 [-4.00; -0.50]	-2.00 [-4.00; 0.50]
	p	0.386	0.349	0.014
Emotional aspects	Study group	-1.00 [-2.00; 0.00]	-1.00 [-2.00; 0.00]	-3.00 [-4.25; -1.00]
	Control group	-1.00 [-2.00; 0.00]	-1.00 [-2.50; 0.00]	-1.00 [-3.00; 1.00]
	p	0.407	0.927	< 0.001

Note. [Q1; Q3]—interquartile range; p—level of statistical significance; V0—QoL assessment before surgery; V1—QoL assessment 5 days after surgery; V2—QoL assessment 1 month after surgery; V3—QoL assessment 1 year after surgery. Statistically significant differences ($p < 0.05$) are highlighted in bold.

stage (375.0 [320.0–440.0]) and 1 year later (397.5 [340.0–430.0]) (p=0.011), compared with the control group, where no statistically significant changes were found (p=0.229). An analysis of the dependence of hospitalizations on the distance walked by patients during the 6MWT was performed, and in the group of patients without rehospitalizations, a statistically significant improvement in the 6MWT indicator was noted (p=0.004).

When analyzing echocardiography data without dividing into groups, no statistically significant differences were obtained (Table 4).

An analysis of intergroup differences at the pre-operative stage and 1 year after surgery was performed. No statistically significant changes were found for any parameters except for the size of the right atrium before surgery and at 1 year.

When analyzing the MLHFQ scores, it turned out that there was an improvement in well-being according to the "Total" score: before surgery, the median was 21.00 points (13.00–30.50), at 5 days—14.00 points (10.00–24.00), at 1 month—14 points (8.00–20.00), at 1 year—12 points (7.00–19.50). The differences were statistically significant at all stages compared to the pre-operative period (p<0.001).

It was also found that patients in the study and control groups had significant differences at the pre-operative stage in the total QoL score and the "Economic Aspects" and "Emotional Aspects" subscales. For them, an analysis of the absolute increase/decrease in questionnaire scores was performed (Table 5).

It was found that both in the total QoL score and in individual subscales, there was a decrease in the number of points, indicating an improvement in QoL. When analyzing by groups, it was found that the study group had a statistically significantly greater decrease in the total score and the "Economic Aspects" and "Emotional Aspects" subscales after one year compared to the control group (p=0.002; p=0.014; p<0.001, respectively).

For the "Physical Capacity" subscale, in which the groups were initially comparable, over the entire study period, a statistically significant improvement in QoL was found in both the study and control groups (p<0.001).

Discussion

The conducted study allows for a comprehensive assessment of the impact of remote monitoring on the course of CHF and QoL in elderly patients after implantation of dual-chamber pacemakers.

At the same time, we did not find statistically significant differences in the frequency of hospitalizations between the study and control groups (27.5% vs. 23.6%; p=0.669). The structure of hospitalization causes was also comparable. This suggests that RM, at least in this study, did not lead to a greater reduction in hospitalization rates compared to standard in-person follow-up. This result is consistent with the meta-analysis that summarized data from 15 studies,

which also did not reveal a significant effect of RM on mortality, but differs from the data of the HERO study, in which patients with pacemakers under remote monitoring showed a reduction in unplanned healthcare contacts, although the overall hospitalization rate remained comparable [8, 11]. However, it is important to note that in our study, the study group had more patients with two or more hospitalizations (5 vs. 3), which may indicate a more complex patient population or more active detection and hospitalization of decompensated conditions.

Our study showed a significant decrease in CSAS scores one year after surgery compared to the pre-operative level in the entire patient cohort ($p<0.001$) and separately in each group, confirming an objective improvement in clinical symptoms of CHF after pacemaker implantation regardless of the follow-up method. A significant increase in 6MWT distance after one year was observed both in the overall patient sample ($p=0.007$) and separately in the study group ($p=0.011$), which confirms the literature data on better adaptation to physical activity after device implantation [12]. A possible explanation for the results obtained is that regular RM contributed to better treatment adherence.

Echocardiography did not reveal significant dynamics of key indicators of cardiac structure and systolic function one year after surgery, neither in the overall group nor when divided into study and control groups. These data are similar to the results of the single-center COMMIT-HF study with 822 patients [13].

The improvement in QoL in our study is consistent with the long-term results of LopezVillegas et al., who observed a sustained positive effect of remote monitoring on quality of life and patient satisfaction with implanted pacemakers over five years [14].

Furthermore, the identified relationship between lower QoL scores (total score and "Economic" and "Emotional Aspects" subscales) and an increased risk of rehospitalization in the study group is of interest. These data may indicate that subjective assessment of well-being, especially in the economic and emotional spheres, can serve as a predictor of decompensation in patients under remote monitoring.

Conclusion

Pacemaker implantation in patients over 60 years of age is accompanied by a statistically significant improvement in clinical status, functional status, and quality of life, regardless of the follow-up method. At the same time, a significant increase in 6MWT distance over the year was recorded only in the remote monitoring group, highlighting the advantage of remote monitoring in terms of exercise tolerance. The comparable hospitalization rate and the absence of significant dynamics in echocardiographic parameters in both groups allow considering remote monitoring as an effective and safe approach to managing this category of patients.

Study Limitations. Only one questionnaire was used to assess quality of life; data transmission was performed using a single specific telemetry system ("CareLink Network," Medtronic, USA); effectiveness and patient acceptability may vary depending on the technological platform and interface used; the follow-up period was 1 year, which does not allow assessing the long-term impact on prognosis, structural changes in the heart, and the sustainability of functional status improvement.

Conflict of interest: none declared.

Литература/References

1. Fatenkov OV, D'yachkov VA, Kshnyakin PA, et al. Decade of Remote Monitoring for Patients with Chronic Heart Failure: An Analysis of Publications on the Use of Telemedicine Technologies. Bulletin of the Medical Institute "REAVIZ" (REHABILITATION, DOCTOR AND HEALTH). 2025;15(2):105–112. Russian. DOI:10.20340/vmi-rvz.2025.2.CLIN.6
2. Klein L. Current and future landscape of remote hemodynamic monitoring. J Card Fail. 2025;31(11):1731-1742. DOI: 10.1016/j.cardfail.2025.09.007
3. Pyrikova NV, Mozgunov NA, Osipova IV. Results of pilot remote monitoring of heart failure patients. Cardiovasc. Ther. Prev. 2022;21(6):42–51. Russian. DOI:10.15829/1728-8800-2022-3151
4. Pravkina EA, Pereverzeva KG, Budanova IV, et al. Telemedicine: Definition, Implementation Features, Effectiveness and Prospects for Use in Cardiology. Science of the young (Eruditio Juvenium). 2023;11(3):435–446. Russian. DOI:10.23888/HMJ2023113435-446
5. Ihala Gamage S, Chathuranga T, Dahanayake N. Pacing-Induced Cardiomyopathy Following Permanent Pacemaker Implantation: A Case Report and Review of Management

Strategies. Cureus. 2025;17(8):e90624. DOI: 10.7759/cureus.90624

6. Grachev DS, Petrov VS, Namazova KI, et al. Vascular Stiffness in Senile Patients with Chronic Heart Failure. I. P. Pavlov Russian Medical Biological Herald. 2024;32(1):65–72. Russian. DOI: 10.17816/PAVLOVJ375266
7. Aringazina RA, Khamidulla BKh, Abenova N, et al. Resynchronizing Implantable Cardioverter-Defibrillator (CRT-D) for Left Ventricular Dysfunction in Patients with Chronic Heart Failure. West Kazakhstan Medical Journal. 2024;4. Russian. DOI: 10.18502/wkmj.v66i4.17778
8. Ezimoha K, Faraj M, Kanduri Hanumantharayudu S, et al. The impact of remote patient monitoring on clinical outcomes in heart failure patients: A Meta-Analysis. Cureus. 2025;17(9):e92812. DOI: 10.7759/cureus.92812
9. Calvanese R, D'Amore C, Capobianco C, et al. Integrating Remote CIED Monitoring into Heart Failure Care: Evidence, Challenges, and Opportunities. Front Cardiovasc Med. 2026;Article 1734567. DOI: 10.3389/fcvm.2026.1734567
10. Kotsoeva OT, Tyrenko VV, Koltcov AV, et al. Evaluation of the dynamics of the quality of life in patients with chronic heart failure during therapy. Cardiology: News, Opinions, Training. 2022;10(3):26–35. Russian. DOI:10.33029/2309-1908-2022-10-3-26-35
11. Adriaansen E, Theuns DAMJ, Kuijper AFM, et al. Remote monitoring in pacemaker patients: the HERO study. Neth Heart J. 2025;33(6):184–185. DOI: 10.1007/s12471-025-01957-0
12. Spaggiari CV, de Siqueira SF, de Oliveira CP, et al. Feasibility of physiological pacing rate in cardiac resynchronization therapy. ESC Heart Fail. 2023;10(4):2751-2753. DOI: 10.1002/ehf2.14429
13. COMMIT-HF Investigators. Alert Transmissions From Remote Monitoring of Patients With Cardiac Implantable Devices: Long-Term Results From the COMMIT-HF Registry. JACC Clin Electrophysiol. 2023;9(10):2163-2165. DOI: 10.1016/j.jacep.2023.07.005
14. Lopez-Villegas A, Catalan-Matamoros D, Robles-Musso E, et al. A non-randomized clinical trial to examine patients' experiences and communication during telemonitoring of pacemakers after five years follow-up. PLoS One. 2021;16(2):e0246170. DOI: 10.1371/journal.pone.0246170

International Heart and Vascular Disease Journal. Volume 14, № 50, June 2026
ISSN: 2311-1623 (Print)
ISSN: 2311-1631 (Online)
http://www.heart-vdj.com

Cardiovascular risk with long-term use of proton pump inhibitors

Trukhan D.I.

Federal State Budgetary Institution of Higher Education "Omsk State Medical University" of the Ministry of Health of the Russian Federation, Omsk, Russia.

AUTHOR

Dmitry I. Trukhan*, PhD, MD, Associate Professor, Professor of the Department of Polyclinic Therapy and Internal Diseases, Federal State Budgetary Educational Institution of Higher Education "Omsk State Medical University" of the Ministry of Health of the Russian Federation, Omsk, Russia. ORCID: 0000-0002-1597-1876

Proton pump inhibitors (PPIs) are the most effective drugs for the treatment of acid-dependent diseases. From gastroenterological practice, PPIs are being actively introduced into other specialties, particularly cardiology and rheumatology, where they are used to protect the gastrointestinal mucosa and prevent gastrointestinal bleeding during long-term antithrombotic therapy and long-term use of nonsteroidal anti-inflammatory drugs.

Objective of this review is to present and analyze data from international and national studies on the presence of cardiovascular risk with long-term PPI use.

Material and methods. The article uses materials from peer-reviewed articles published in PubMed, Scopus, and e-library.ru from 2013 to 2025 using the keywords: proton pump inhibitors, cardiovascular risk, myocardial infarction, arterial hypertension, stroke, arrhythmias, rhabdomyolysis.

Results. In the current decade, a number of international reviews have been published examining the associations between long-term PPI use and a range of diseases/conditions, including the cardiovascular risk associated with their use. The data presented in the review suggest a possible association between long-term PPI use and the development of myocardial infarction, arterial hypertension, stroke, and cardiac arrhythmias.

Conclusion. Increasing awareness among physicians and patients about the appropriate use of PPIs and knowledge of the adverse effects of long-term therapy will optimize the use of these drugs in real clinical practice, especially in comorbid patients with cardiovascular disease.

Keywords: proton pump inhibitors, cardiovascular risk, myocardial infarction, arterial hypertension, stroke, arrhythmias, rhabdomyolysis.

Conflict of interest: none declared.

Received: 27.02.2026
Accepted: 04.05.2026

* Corresponding author. Tel. +7 (381) 295-72-77. E-mail: dmitry_trukhan@mail.ru

For citation: Trukhan D.I. Cardiovascular risk with long-term use of proton pump inhibitors. International Heart and Vascular Disease Journal. 2026. 14(50): 41-48. DOI: 10.24412/2311-1623-2026-50-48-56

Introduction

Cardiovascular diseases (CVDs) occupy a leading place in the structure of chronic noncommunicable pathology in the adult population and are the main cause of premature death and early disability in most economically developed countries. In the Russian Federation, according to Rosstat, in 2023 the total number of deaths due to diseases of the circulatory system was 814.4 thousand people, which corresponds to 46% of all cases.

Proton pump inhibitors (PPIs) are considered the most effective drugs for the treatment of acidrelated diseases. In recent decades, the use of PPIs has grown exponentially [1]. From gastroenterological practice, PPIs are being actively introduced into other specialties, in particular cardiology and rheumatology, where they are used to protect the gastrointestinal mucosa and prevent gastrointestinal bleeding during longterm antithrombotic therapy and longterm use of nonsteroidal antiinflammatory drugs (NSAIDs).

Since the appearance of the first PPI, omeprazole, on the pharmaceutical market (1988), for a long period of time PPIs were considered safe drugs for shortterm and longterm use [2]. However, current clinical guidelines note that when prescribing PPIs in high doses for a long period, the possibility of adverse effects should be considered. In recent years, a number of international reviews have been published that examine the associations between PPIs and various diseases/conditions, including the possible association of PPI use with an increased risk of cardiovascular complications.

The aim of this review article is to present and analyze data from international and national studies on the possible presence of cardiovascular risk (CVR) with longterm use of PPIs.

Material and methods

In preparing this article, materials from peerreviewed articles published in PubMed, Scopus and e-library.ru from 2013 to 2025 were used, using the keywords: proton pump inhibitors, cardiovascular risk, myocardial infarction, arterial hypertension, stroke, cardiac arrhythmias, rhabdomyolysis.

Results

Proton pump inhibitors and overall cardiovascular risk

Increased CVR with longterm PPI use may be related to a number of factors: increased plasma levels of asymmetric dimethylarginine (ADMA), which reduces nitric oxide (NO) production in vessels by competitively inhibiting nitric oxide synthase (NOS) [3]; endothelial dysfunction, hypomagnesaemia and hypocalcaemia, decreased levels of vitamins C and B12 [4, 5]. Longterm PPI use may result in endothelial cell dysfunction, accelerated endothelial ageing, increased oxidative stress, hyperinflammation and premature vascular ageing [6]. Examples of this relationship are shown in several studies.

For example, in the US ARIC (Atherosclerosis Risk in Communities) study involving 4,436 participants, patients taking PPIs [7] more often had hypomagnesaemia (≤0.75 mmol/L) (hazard ratio (HR) 1.24; 95% confidence interval (CI) 1.081.44); during a 5 year follow up, 684 cases of CVD occurred. PPI users had a higher risk of CVD (HR 1.31; 95% CI 1.10–1.57) than nonusers.

In a retrospective Thai cohort study of 3,928 patients taking PPIs and 3,928 patients taking H2antihistamines [8], an association was found between PPI use and CVD (HR 1.76; 95% CI 1.40–2.20), ischaemic stroke (IS) (HR 3.53; 95% CI 2.21–5.64) and peripheral vascular disease (HR 17.07; 95% CI 13.82–76.25) compared with H2antihistamine use. The association between PPIs and each outcome was significant with a medication possession ratio >50%. Furthermore, the association between PPIs and diseases of the circulatory system was robust to unmeasured confounders (e.g., smoking and alcohol).

A ChineseAmerican prospective cohort study [9] demonstrated an association between regular PPI use and cardiovascular outcomes (459,207 participants without CVD were identified). Over a follow-up of more than 8 years, the researchers recorded 26,346 cases of CVD (including 13,749 cases of coronary heart disease (CHD), 4,144 cases of stroke, 5,812 cases of atrial fibrillation (AF), 1,159 cases of heart failure (HF), and 4,206 cases of venous throm-

boembolism). Fully adjusted hazard ratios (AHRs) in PPI users were elevated compared with nonusers and were noted for all CVD events (AHR 1.44; 95% CI 1.39–1.50), for CHD (AHR 1.65; 95% CI 1.57–1.74), for stroke (AHR 1.21; 95% CI 1.09–1.33), for AF (AHR 1.17; 95% CI 1.08–1.28), for HF (AHR 1.61; 95% CI 1.37–1.89) and for venous thromboembolism (AHR 1.36; 95% CI 1.24–1.50). The researchers note that regular PPI use was associated with higher CV risk, and therefore caution is needed when prescribing PPIs.

In an Italian populationbased cohort study of 284,068 patients (49.4% PPI users, 50.6% nonusers) [10], the risk of CVD and death in elderly people with diabetes mellitus (DM) was studied. Over a median followup of 6.7 years, PPI use was associated with a higher risk of IS (HR 1.14; 95% CI 1.08–1.20), myocardial infarction (MI) (HR 1.36; 95% CI 1.31–1.41) and allcause mortality (HR 1.24; 95% CI 1.22–1.26). These risks were elevated regardless of the specific PPI agent used.

According to a metaanalysis (17 studies, 7,540 participants) conducted by Chinese pharmacologists and gastroenterologists [11], patients taking PPIs had a 70% higher risk of major cardiovascular events (HR 1.70; 95% CI 1.132.56; p=0.01). The highest risk of adverse cardiovascular events was noted in the subgroup of longterm PPI use (HR 2.33; 95% CI 1.334.08; p=0.003) and in those taking omeprazole (HR 3.17; 95% CI 1.437.03; p=0.004).

In a metaanalysis of 11 studies by Chinese cardiologists [12], clopidogrel monotherapy (55,494 patients) was compared with clopidogrel + PPI therapy (29,235 patients). Patients taking PPIs had an increased risk of major adverse cardiovascular events (odds ratio (OR) 1.37; 95% CI: 1.23–1.53; p <0.00001), MI (OR 1.41; 95% CI: 1.26–1.57; p <0.00001), target vessel revascularization (OR 1.28; 95% CI: 1.011.61; p = 0.04) and stent thrombosis (OR 1.38; 95% CI: 1.13–1.70; p = 0.002). In another metaanalysis of 15 studies involving 50,366 patients, Chinese cardiologists demonstrated [13] that patients not taking PPIs had a significantly reduced risk of major adverse cardiovascular events (MACE) (HR 0.82; 95% CI 0.770.88), stroke (HR 0.72; 95% CI 0.670.76), recurrent MI (HR 0.72; 95% CI 0.570.90), target vessel revascularization (HR 0.77; 95% CI 0.630.93) and stent thrombosis (HR 0.71; 95% CI 0.560.92).

American scientists studied 85,189 postmenopausal women (mean age 63 years at baseline) without known CVD at enrolment in the observational Women's Health Initiative study [14]. At baseline, 1,747 (2.1%) women reported PPI use. Over a mean followup of 11 years, 5,778 (6.8%) cases of primary CVD were identified. In patients taking PPIs, the risk of developing CVD was significantly higher than in those not taking them (HR 1.21; 95% CI: 1.02–1.43). Longer PPI use was associated with a gradually increasing risk of CVD (HR <1 year: 1.11; 1–3 years: 1.27; >3 years: 1.33; p = 0.02).

Proton pump inhibitors and myocardial infarction

The increased risk of MI may be related to elevated ADMA levels, which block the enzyme dimethylarginine dimethylaminohydrolase (DDAH). NOS is blocked by ADMA, leading to decreased NO production, enhanced vasoconstriction and reduced vasodilation [15].

In a Taiwanese cohort study of 27,624 patients using PPIs who subsequently developed acute MI (AMI) and 27,624 control subjects using PPIs but without subsequent AMI or CHD, it was shown [16] that longterm PPI use or highdose PPI use increased the risk of firstever AMI in patients (OR 1.56; 95% CI 1.45–1.69) without a history of CHD. The Taiwanese scientists noted that the increased risk of AMI was associated with the use of all PPIs studied (omeprazole, esomeprazole, rabeprazole, pantoprazole and lansoprazole). In a US casecontrol study of 32,793 patients taking PPIs who developed AMI and 127,291 control patients without AMI, individuals who started PPI therapy [17] had an increased risk of MI (adjusted OR (AOR) 2.8; 95% CI 2.63.0).

In a recently published retrospective analysis by Chinese cardiologists [18], data from the US National Health and Nutrition Examination Survey (NHANES) for 20072018 were used. In a cross-sectional analysis of data from 47,713 US adults, PPI use was positively associated with the risk of MI (OR 1.668; 95% CI 1.224–2.273; p <0.001). Subgroup analysis showed that men and smokers were more susceptible to MI risk associated with longterm PPI use [18].

Proton pump inhibitors and arterial hypertension

Japanese and French scientists studied the potential association between PPIs and arterial hypertension (AH) using the WHO pharmacovigilance database

DOI: 10.24412/2311-1623-2026-50-48-56

[19]. The database contained 26,587 reports of AH associated with PPIs (2.3%), predominantly in women (63.3%). A significant reporting odds ratio (ROR) was observed for almost all PPIs in both univariate (ROR 1.32–1.97) and multivariate analyses after adjustment for confounders (adjusted ROR 1.09–1.35). A potential trend indicating a doseeffect relationship was identified: doses below the median were associated with a lower adjusted ROR for AH [19].

In a study by a group of American scientists involving 64,720 menopausal women without CVD or AH at baseline, 28,951 cases of AH were recorded after a mean followup of 8.7 years [20]. PPI use was associated with a 17% increased risk of AH compared with nonusers in the fully adjusted model (HR 1.17; 95% CI 1.08–1.27). Longer PPI use was significantly associated with a gradually increasing risk of AH (HR 1.13; 1.17; 1.28 respectively; p for trend <0.001). The 3year change in mean systolic blood pressure adjusted for multivariate factors significantly increased in new PPI users (+3.39 mm Hg; p = 0.049) compared with those who never used these drugs. Thus, PPI use was associated with an increased risk of developing AH in menopausal women, and the risk showed a significant trend towards increasing with duration of use [20].

Proton pump inhibitors and stroke

Longterm PPI use increases the risk of stroke by raising plasma ADMA levels and reducing NO levels [21]. Neurologists from South Korea, in a multivariate Cox regression analysis, demonstrated an association between longterm PPI use and the development of cerebral small vessel disease and deep white matter hyperintensity, which may be a cause of stroke or cognitive decline (HR 3.453; 95% CI 1.027–9.475; p = 0.045) [22].

In a Danish nationwide retrospective cohort study of 214,998 individuals, over a median followup of 5.8 years, 7,916 cases of IS and 5,608 cases of MI were recorded. The risk of firstever IS (HR 1.13; 95% CI 1.08–1.19) and MI (HR 1.31; 95% CI 1.23–1.39) was elevated in PPI users [23]. High doses of PPIs were associated with an increased incidence of IS (HR 1.31; 95% CI 1.21–1.42) and MI (HR 1.43; 95% CI 1.30–1.57). Longterm PPI use, compared with nonusers, increased the risk of IS by 29% (95% CI 559%) and the risk of MI by 36% (95% CI 773%) over 6 months. H2antihistamine use was not significantly associated with IS (HR 1.02; 95% CI 0.84–1.24) or MI (HR 1.15; 95% CI 0.92–1.43) [23]. In a Taiwanese retrospective nationwide cohort study using 198,148 courses of PPI therapy and control periods without PPI use, PPI use was positively associated with an increased risk of hospitalisation for IS (HR 1.36; 95% CI 1.14–1.620; p=0.001) [24]. In a nested casecontrol analysis, Taiwanese neurologists and gastroenterologists identified 15,378 patients hospitalised for IS and compared them with matched controls (n=15,378); an association was found between PPI use and elevated cerebrovascular risk within 30 days (AOR 1.77; 95% CI 1.45–2.18; p<0.001), within 3190 days (AOR 1.65; 95% CI 1.31–2.08; p<0.001), and within 91180 days (AOR 1.28; 95% CI 1.03–1.59; p=0.025) from the start of PPI therapy to the first IS [24].

In a prospective analysis by Chinese scientists among 492,479 participants from the UK Biobank, over a followup of 3,935,030 personyears, 5,182 cases of stroke were documented [25]. Regular PPI use was associated with a 16% increased risk of stroke compared with nonusers (HR 1.16; 95% CI 1.06–1.27). This result was close to the results of a metaanalysis of nine randomised controlled trials (events/participants 371/26,642; HR 1.22; 95% CI 1.001.50) conducted by the authors. In a metaanalysis by Chinese cardiologists (14 studies) [26], PPI users had a higher risk of stroke (OR 1.22; 95% CI 1.08–1.36), MI (OR 1.23; 95% CI 1.14–1.32), MACE (OR 1.22; 95% CI 1.05–1.40) and cardiovascular death (OR 1.83; 95% CI 1.69–1.98).

Proton pump inhibitors and cardiac arrhythmias

Chinese cardiologists conducted a study to determine the association between PPI treatment and QT interval prolongation in critically ill patients [27]. The study included 24,512 intensive care unit patients. Of these, 11,327 patients received PPIs (group 1), 4,181 received H2antihistamines (group 2), and 6,351 had no acidsuppressive therapy (group 3); the frequency of QT prolongation in the groups was 8.5%, 3.3% and 3.4%, respectively. After adjustment for confounders, PPI use was associated with a higher risk of QT prolongation compared with H2antihistamines (OR 1.66; 95% CI 1.36–2.03) and compared with no acidsuppressive therapy (OR 1.54; 95% CI 1.31–1.82). Two drugs, pantoprazole (OR 2.14; 95% CI 1.52–3.03) and lansoprazole (OR 1.80; 95% CI 1.18–2.76), showed a higher risk of QT prolongation than omeprazole.

Concomitant medications conferred a higher risk of QT prolongation when combined with PPI use.

In a DanishDutch study, it was found that PPI use was associated with an increased risk of outofhospital sudden cardiac arrest (SCA) [28]. The authors identified 46,578 cases of SCA and 232,890 control individuals without a history of SCA. PPIs were used by 8,769 patients with SCA and 21,898 patients without SCA in the control group. Current PPI use increased the odds of SCA compared with nonusers (OR 1.32; 95% CI 1.28–1.37). The risk remained elevated in individuals without registered CHD (OR 1.36; 95% CI 1.31–1.41), without HF (OR 1.33; 95% CI 1.29–1.38) or without any concomitant CVD (OR 1.84; 95% CI 1.70–2.00).

Furthermore, a close association of longterm PPI use with important cardiovascular risk factors such as DM [29] and chronic kidney disease (CKD) [30] has been noted.

Proton pump inhibitors and rhabdomyolysis

During the search for sources addressing PPI adverse effects, several clinical cases reporting the development of rhabdomyolysis in individuals taking PPIs were found. This rare adverse effect has been described with all major representatives of the PPI class: omeprazole, esomeprazole, rabeprazole, pantoprazole and lansoprazole [31, 32]. In the description of the active substances of the main PPI representatives, rhabdomyolysis is not listed among the adverse effects. In cardiological practice, it is known that rhabdomyolysis is a serious adverse reaction to HMGCoA reductase inhibitors (statins) [33]; however, in the "drug interactions" section for the main PPI representatives, the interaction of PPIs with statins is not addressed.

Japanese pharmacologists and gastroenterologists analyzed two databases: the Japanese Medical Data Vision (MDV) and the US FDA Adverse Event Reporting System (FAERS) [34]. Multiple logistic regression analysis of both databases showed a significant association between PPI use and an increased risk of rhabdomyolysis (OR 1.84, 95% CI 1.74–1.95, $p \leqslant 0.01$). H2antihistamine use was not significantly associated with an increased risk of rhabdomyolysis. Pharmacologists from Saudi Arabia also used the FDA FAERS database for the period 20132021 [35]. The authors found 57 reports linking PPIs to rhabdomyolysis out of 3,670 reports for other drugs (including nonstatins). The association between rhabdomyolysis and PPIs was significant in reports both including statins (ROR 2.0; 95% CI 1.5–2.6) and excluding statins (ROR 2.5; 95% CI 1.9–3.2). Chinese pharmacologists in the FDA FAERS database analyzed 1,899 reports with complete patient demographic data [31]. Lansoprazole had the highest ROR—12.67, followed by esomeprazole (11.18), omeprazole (10.27), rabeprazole (10.06) and pantoprazole (9.24). In cases of rhabdomyolysis, PPIs were mainly "concomitant" drugs (>60%), and only a few cases were "primary suspects" (<15%). Rabeprazole showed the lowest mortality rate, while lansoprazole had the highest. American gastroenterologists [36] note that in the development of rhabdomyolysis with PPI use, their interaction with coadministered drugs such as statins may be involved. In patients who recover from an episode of PPIassociated rhabdomyolysis but have no real need to continue PPIs, rechallenge is not advisable. In those with clear indications for continued PPI treatment, PPIs may be resumed, but it is advisable not to prescribe them together with statins.

Discussion

In realworld clinical practice, longterm PPI use refers to their use for more than 4 weeks in gastric diseases (peptic ulcer and functional dyspepsia) and for more than 8 weeks in oesophageal diseases [37]. This review presents data suggesting a possible association between longterm PPI use and the development of MI, AH, stroke and cardiac arrhythmias.

A review by American cardiologists notes that since longterm PPI use may increase the risk of CVD, the benefits of PPIs must be carefully weighed against the potential risks for each patient [38]. Alternative treatments may be used for individuals at high CV risk.

To date, the attitude towards using PPIs for gastrointestinal mucosal protection and prevention of gastrointestinal bleeding during longterm antithrombotic therapy in cardiological practice is controversial. A review by American cardiologists [39] notes that in patients with CVD receiving dual antiplatelet therapy (DAPT), drug interactions between clopidogrel and PPIs may lead to worse cardiovascular outcomes [12]. A multicentre Chinese study [40] included 25,567 patients with acute coronary syndrome (ACS) receiving DAPT. PPIs were prescribed within 24 hours of admission to 63.9% (n=16,332) of patients. A higher

rate of gastrointestinal bleeding was noted in PPI users compared with nonusers (1.0% vs. 0.5%; p<0.001). In a multivariate Cox regression analysis, early PPI use was associated with a 58% increased risk of gastrointestinal bleeding (HR 1.58; 95% CI 1.15–2.18; p=0.005). A South Korean multicentre observational study determined the risk of lower gastrointestinal bleeding and compared this risk between NSAID+PPI users (target cohort, n=24,530) and NSAIDonly users (comparison cohort, n=57,264) [41]. The risk of lower gastrointestinal bleeding was significantly higher in the target cohort (NSAID+PPI) than in patients taking NSAIDs alone (HR 2.843; 95% CI 1.998–4.044; p < 0.001). Similar results were noted in subgroups—elderly patients >65 years (HR 2.737), men (HR 2.963) and women (HR 3.221).

Consensuses of Russian experts on antithrombotic therapy in elderly and senile age [42] and on reducing the risk of gastrointestinal bleeding in patients receiving oral anticoagulants [43] note that a significant drawback of PPIs is their inability to prevent erosiveulcerative lesions of the lower gastrointestinal tract associated with antiplatelet and anticoagulant use. Moreover, PPI use, on the contrary, increases the risk of enteropathy, may enhance damage to the small intestinal mucosa (especially when combined with NSAIDs), and may even provoke lower gastrointestinal bleeding. In this regard, it is advisable to use gastroprotective agents with a mechanism of action different from that of PPIs, for example rebamipide.

Recent reviews have formulated the main principle of PPI therapy safety: prescribing PPIs strictly according to indications (in accordance with clinical guidelines), adhering to short courses and minimal effective doses [44, 45].

Conclusion

The conducted literature analysis suggests a possible association between longterm PPI use and the development of MI, AH, stroke and cardiac arrhythmias. During the review of the literature, an unexpected serious adverse reaction associated with PPI use—rhabdomyolysis—was identified.

This review article indicates the possibility and reality of cardiovascular risk with longterm PPI use, and that this should be taken into account when prescribing PPIs for a long period, especially in comorbid patients. Increasing awareness among physicians and patients about the proper use of PPIs and knowledge of the adverse effects of longterm therapy will optimize the use of these drugs in realworld clinical practice.

Conflict of interest: none declared.

Литература/References

1. Al-Aly Z, Maddukuri G, Xie Y. Proton pump inhibitors and the kidney: implications of current evidence for clinical practice and when and how to deprescribe. Am J Kidney Dis 2020;75:497–507. DOI: 10.1053/j.ajkd.2019.07.012
2. Novotny M, Klimova B, Valis M. PPI Long Term Use: Risk of Neurological Adverse Events? Front Neurol. 2019; 8;9:1142. DOI: 10.3389/fneur.2018.01142
3. Smith CA, Ebrahimpour A, Novikova L et al. Esomeprazole covalently interacts with the cardiovascular enzyme dimethylarginine dimethylaminohydrolase: Insights into the cardiovascular risk of proton pump inhibitors. Biochim Biophys Acta Gen Subj. 2022; 1866(8):130149. DOI: 10.1016/j.bbagen.2022.130149
4. Ariel H, Cooke JP. Cardiovascular risk of proton pump inhibitors. Methodist Debakey Cardiovasc J. 2019;15:214–219. DOI: 10.14797/mdcj-15-3-214
5. Koyyada A. Long-term use of proton pump inhibitors as a risk factor for various adverse manifestations. Therapie. 2021; 76(1):13-21. DOI: 10.1016/j.therap.2020.06.019
6. Nochaiwong S, Ruengorn C, Awiphan R et al. The association between proton pump inhibitor use and the risk of adverse kidney outcomes: a systematic review and meta-analysis. Nephrol Dial Transplant. 2018;33:331–342. DOI: 10.1093/ndt/gfw470
7. Rooney MR, Bell EJ, Alonso A et al. Proton pump inhibitor use, hypomagnesemia and risk of cardiovascular diseases: the atherosclerosis risk in communities (ARIC) Study. J Clin Gastroenterol. 2021; 1;55(8):677-683. DOI: 10.1097/MCG.0000000000001420
8. Pannoi T, Promchai C, Apiromruck P et al. Risk of circulatory diseases associated with proton-pump inhibitors: a retrospective cohort study using electronic medical records in Thailand. PeerJ. 2024; 15;12:e16892. DOI: 10.7717/peerj.16892
9. Li ZH, Zhong WF, Qiu CS et al. Association between regular proton pump inhibitors use and cardiovascular outcomes: A large prospective cohort study. Int J Cardiol. 2024; 15;395:131567. DOI: 10.1016/j.ijcard.2023.131567
10. Foresta A, Fernandez LO, Torrigiani G et al. Proton pump inhibitor use and the risk of cardiovascular complications and death in older adults with diabetes: a population-based cohort Study.Drugs Aging. 2024;41(3):239-249. DOI: 10.1007/s40266-024-01097

11. Sun S, Cui Z, Zhou M et al. Proton pump inhibitor monotherapy and the risk of cardiovascular events in patients with gastro-esophageal reflux disease: a meta-analysis. Neurogastroenterol Motil. 2017;29:e12926. DOI: 10.1111/nmo.12926
12. Bundhun PK, Teeluck AR, Bhurtu A, Huang WQ. Is the concomitant use of clopidogrel and proton pump inhibitors still associated with increased adverse cardiovascular outcomes following coronary angioplasty?: a systematic review and meta-analysis of recently published studies (2012- 2016). BMC Cardiovasc Disord. 2017;17:3. DOI: 10.1186/s12872-016-0453-6
13. Pang J, Wu Q, Zhang Z et al. Efficacy and safety of clopidogrel only vs. clopidogrel added proton pump inhibitors in the treatment of patients with coronary heart disease after percutaneous coronary intervention: a systematic review and meta-analysis. Int J Cardiol Heart Vasc. 2019; 23:100317. DOI: 10.1016/j.ijcha.2018.12.016
14. Soliman AI, Wactawski-Wende J, Millen AE et al. Proton pump inhibitor use and incident cardiovascular disease in older Postmenopausal Women.J Am Geriatr Soc. 2025; 73(2):411-421. DOI: 10.1111/jgs.19326
15. Freedberg DE, Yang YX, Abrams JA. Proton pump inhibitors and myocardial infarction. Gastroenterology. 2015;149:830–833. DOI: 10.1053/j.gastro.2015.08.002
16. Tseng HJ, Cheng CM, Tsai SJ et al. Proton pump inhibitor exposure and acute myocardial infarction risk: a nested cohort study. Cardiovasc Toxicol. 2021; 21:444–450. DOI: 10.1007/s12012-021-09637-2
17. Qian Y, Jick S. Proton-pump inhibitor use and myocardial infarction: a nested case-control study in the UK Clinical Practice Research Datalink. Epidemiology. 2020; 31:423–431. DOI: 10.1097/EDE.0000000000001152
18. Zhang W, Yuan Z, Zhou J. Association between proton pump inhibitor use and the risk of myocardial infarction: A cross-sectional study based on NHANES 2007 to 2018. Medicine (Baltimore). 2025; 29;104(35):e44030. DOI: 10.1097/MD.0000000000044030
19. Chretien B, Cacquevel M, Kazuki N et al. Association between exposure to proton pump inhibitors and hypertension: a descriptive and disproportionality analysis of VigiBase. BMJ Open. 2025; 27;15(11):e105962. DOI: 10.1136/bmjopen-2025-105962
20. Soliman AI, Wactawski-Wende J, Millen AE, Gray SL, Eaton CB, et al. Proton pump inhibitor use and incident hypertension in menopausal women. J Am Heart Assoc. 2025 ; 14(13):e040009. DOI: 10.1161/JAHA.124.040009
21. Ghebremariam YT, LePendu P, Lee JC et al. Unexpected effect of proton pump inhibitors: elevation of the cardiovascular risk factor asymmetric dimethylarginine. Circulation. 2013; 128:845–853. DOI: 10.1161/CIRCULATIONAHA.113.003602
22. Kang MK, Shin JH, Kim TJ et al. Use of proton pump inhibitor may be associated with progression of cerebral small vessel disease. PLoS One. 2022;17:e0279257. DOI: 10.1371/journal.pone.0279257
23. Sehested TSG, Gerds TA, Fosbøl EL et al. Long-term use of proton pump inhibitors, dose-response relationship and associated risk of ischemic stroke and myocardial infarction. J Intern Med. 2018;283:268-281. DOI: 10.1111/joim.12698
24. Wang YF, Chen YT, Luo JC et al. Proton-pump inhibitor use and the risk of first-time ischemic stroke in the general population: a nationwide population-based study. Am J Gastroenterol 2017;112:1084-1093. DOI: 10.1038/ajg.2017.101
25. 25.Yang M, He Q, Gao F et al. Regular use of proton-pump inhibitors and risk of stroke: a population-based cohort study and meta-analysis of randomized-controlled trials. BMC Med 2021;19:316. DOI: 10.1186/s12916-021-02180-5
26. Li S, Liu F, Chen C et al. Real-world relationship between proton pump inhibitors and cerebro-cardiovascular outcomes independent of clopidogrel. Int Heart J. 2019; 60:910-918. DOI: 10.1536/ihj.18-584
27. Fan W, Liu H, Shen Y, Hong K. The association of proton pump inhibitors and QT interval prolongation in critically Ill patients. Cardiovasc Drugs Ther. 2024; 38(3):517-525. DOI: 10.1007/s10557-023-07425-4
28. Eroglu TE, Coronel R, Gislason GH. Use of proton pump inhibitors is associated with increased risk of out-of-hospital cardiac arrest in the general population: a nested case-control study. Eur Heart J Cardiovasc Pharmacother. 2024; 10(5):413-419. DOI: 10.1093/ehjcvp/pvae020
29. Liang C, Zhang Y. Proton pump inhibitors use and risk of type 2 diabetes mellitus: correlation analysis, prediction model construction, and key genes identification. Front Pharmacol. 2025; 29;16:1580090. DOI: 10.3389/fphar.2025.1580090
30. Trukhan DI, Viktorova IA Side effects of proton pump inhibitors with long-term use: focus on the urinary system. Medical alphabet. 2024;(5):36-42. Russian. DOI: 10.33667/2078-5631-2024-5-36-42
31. Sun Y, Zhang A, Zuo M et al. A pharmacovigilance study of association between proton-pump inhibitors and rhabdomyolysis event based on FAERS database. J Gastroenterol Hepatol. 2023. 14. DOI: 10.1111/jgh.16411
32. Trukhan DI Drug safety: focus on long-term therapy with proton pump inhibitors. Possible cardiovascular risk and rare side effects. Clinical review for general practice. 2024; 5 (3): 111–118. Russian. DOI: 10.47407/kr2023.5.3.00380
33. Sattar S, Tanveer R, Sattar K. Proton pump inhibitors and the risk of rhabdomyolysis: A call for judicious use in Pakistan.J Pak Med Assoc. 2025;75(3):521. DOI: 10.47391/JPMA.21299

34. Mitsuboshi S, Hamano H, Kuniki Y, et al. Proton Pump Inhi bitors and Rhabdomyolysis: Analysis of Two Different Cross-Sectional Databases. Ann Pharmacother. 2023; 57(11):1255-1263. DOI: 10.1177/10600280231156270
35. Altebainawi AF, Alfaraj LA, Alharbi AA et al. Association between proton pump inhibitors and rhabdomyolysis risk: a post-marketing surveillance using FDA adverse event reporting system (FAERS) database. Ther Adv Drug Saf. 2023; 27;14:20420986231154075. DOI: 10.1177/20420986231154075
36. Duncan SJ, Howden CW. Proton pump inhibitors and risk of rhabdomyolysis. Drug saf. 2017;40(1):61-64. DOI: 10.1007/s40264-016-0473-2
37. Haastrup PF, Jarbøl DE, Thompson W et al. When does proton pump inhibitor treatment become long term? A scoping review. BMJ Open Gastroenterol 2021;8:e000563. DOI: 10.1136/bmjgast-2020-000563
38. Duarte GJ, Lopez J, Sosa F, Molina G, Shaban M, et al. Proton pump inhibitors and cardiovascular risk: a critical review. Future Cardiol. 2024; 28:1-16. DOI: 10.1080/14796678.2024.2412910
39. Khawaja M, Thakker J, Kherallah R, Kitakaze M, Jneid H, et al. Antacid therapy in coronary artery disease and heart failure: proton pump inhibitors vs. H2 receptor Blockers. Cardiovasc Drugs Ther. 2024; 38(1):181-189. DOI: 10.1007/s10557-022-07358-4
40. Zhou M, Zhang J, Liu J et al.; CCC-ACS Investigators. Proton pump inhibitors and in-hospital gastrointestinal bleeding in patients with acute coronary syndrome receiving dual antiplatelet therapy. Mayo Clin Proc. 2022; 12:S0025-6196(21)00919-8. DOI: 10.1016/j.mayocp.2021.11.037
41. Lee M, Kim M, Cha JM. Risk of lower gastrointestinal bleeding in nonsteroidal anti-inflammatory Drug (NSAID) and proton pump inhibitor users compared with NSAID-Only Users: A Common Data Model Analysis. Gut Liver. 2025; 15;19(2):243-252. DOI: 10.5009/gnl240247
42. Tkacheva ON, Vorobyeva NM, Kotovskaya YuV et al. Antithrombotic therapy in the elderly and senile age: the consensus opinion of experts of the Russian Association of Gerontologists and Geriatricians and the National Society of Preventive Cardiology. Cardiovascular Therapy and Prevention. 2021;20(3):2847. Russian. DOI: 10.15829/1728-8800-2021-2847
43. Experts consensus on reducing the risk of gastrointestinal bleeding in patients receiving oral anticoagulants. Therapy. 2021; 10: 23–41. Russian. DOI: 10.18565/therapy.2021.10.23-41
44. Andrawes M, Andrawes W, Das A, Siau K. Proton pump inhibitors (PPIs)-An evidence-based review of indications, efficacy, harms, and deprescribing. Medicina (Kaunas). 2025; 31;61(9):1569. DOI: 10.3390/medicina61091569
45. Bolt J, Thompson W, Inglis C. Appropriate use of proton pump inhibitors in older adults: concerns and solutions. Drugs aging. 2025; 21. DOI: 10.1007/s40266-025-01266-6

International Heart and Vascular Disease Journal. Volume 14, № 50, June 2026
ISSN: 2311-1623 (Print)
ISSN: 2311-1631 (Online)
http://www.heart-vdj.com

Some clinical manifestations of Fabry disease, aspects of diagnosis and treatment

Dzhanibekova A.R.[1], Uzdenov M.B.[1], Dzhanibekova L.R.[1,2], Bogatyreva Z.R.[3], Mutchaeva F.M.[1], Tambieva Z.N.[1]

[1] North Caucasus State Academy, Medical Institute, Cherkessk, Russia.
[2] Karachay-Cherkess Republican Clinical Hospital, Cherkessk, Russia.
[3] Stavropol Regional Clinical Hospital, Stavropol, Russia.

AUTHORS

Asiyat R. Dzhanibekova*, PhD, MD, Associate Professor, Department of Internal Medicine, Dean of the Faculty of International Students, Medical Institute, North Caucasus State Academy; Cardiologist, Functional Diagnostics Physician, Cherkessk, Russia. ORCID: 0000-0002-4719-9980

Marat B. Uzdenov, PhD, MD, Director of the Medical Institute, Associate Professor, Head of the Department of Topographic and Pathological Anatomy with a Course in Operative Surgery, North Caucasus State Academy, Cherkessk, Russia. ORCID: 0000-0002-0077-9013

Leila R. Dzhanibekova, PhD, MD, Associate Professor, Department of Internal Medicine, Medical Institute, North Caucasus State Academy; Cardiologist, Head of the Emergency Cardiology Department, Karachay-Cherkess Republican Clinical Hospital; Chief Freelance Cardiologist of the Ministry of Health of the Karachay-Cherkess Republic, Cherkessk, Russia. ORCID: 0009-0003-6535-2744

Zamira R. Bogatyreva, Cardiologist, Stavropol Regional Clinical Hospital, Stavropol, Russia. ORCID: 0000-0002-0076-3276

Fatima M. Mutchaeva, Assistant, Department of Internal Medicine, Medical Institute, North Caucasus State Academy, Cherkessk, Russia. ORCID: 0009-0006-0022-8250

Zaira N. Tambieva, Assistant, Department of Internal Medicine, Medical Institute, North Caucasus State Academy, Cherkessk, Russia. ORCID: 0009-0007-2408-3997

Mitochondrial diseases are considered among the most common genetic metabolic disorders. A special group consists of lysosomal storage diseases, one form of which is Fabry disease (FD). This is a progressive orphan hereditary metabolic disorder linked to the X chromosome, with a mutation occurring in the GLA gene encoding the en-

* Corresponding author. Tel./Тел. +7 9280110271. E-mail: asia.janibekova@mail.ru

zyme α-galactosidase A, resulting in decreased or absent activity of this enzyme, leading to abnormal accumulation of glycophospholipids and metabolic disturbance.
Objective of this review article is to examine current literature on the pathogenesis, factors playing an important role in the disease pathogenesis, diagnostic algorithms and treatment of FD.
Materials and methods. This review article used works by Russian and foreign authors published on internet platforms and in print over the past 10 years.
Results. The review article discusses current literature on clinical manifestations, factors important in disease diagnosis, modern aspects of diagnosis and principles of FD treatment. Recent studies have also added information on the epidemiology of FD.
Conclusion. Diagnosis and treatment of FD have evolved significantly in recent years due to improved patient selection algorithms, progress in laboratory and instrumental diagnostics of the pathology, and increased accessibility of these methods for timely identification of clinical cases. However, a comprehensive understanding of the etiology, pathogenesis and consequently the clinical manifestations of the disease has still not been achieved, leading to late diagnosis and lack of timely pathogenetic therapy. Therefore, further research is needed to elucidate the factors involved in early diagnosis of the disease in patients with FD.
Keywords: hereditary metabolic disorder, lysosomal storage diseases, Fabry disease, epidemiology, α-galactosidase A, enzyme replacement therapy.

Conflict of interest: none declared.

Received: 17.03.2026
Accepted: 18.05.2026

For citation: Dzhanibekova AR, Uzdenov MB, Dzhanibekova LR, et al. Some clinical manifestations of Fabry disease, aspects of diagnosis and treatment International Heart and Vascular Disease Journal. 2026; 14(50): 49-56. DOI: 10.24412/2311-1623-2026-50-57-65

Introduction

In recent years, there has been growing interest in new nosological forms of hereditary monogenic pathology belonging to the group of lysosomal storage disorders (LSDs), with increasing attention being paid to Fabry disease (FD), also known as Anderson-Fabry disease.

FD is a rare, progressive, inherited metabolic disorder caused by mutations in the GLA gene located on the X chromosome, which encodes the enzyme α-galactosidase A (α-Gal A). Consequently, there is an absence or deficiency of its activity, leading to the abnormal accumulation of two types of phospholipids: primarily globotriaosylceramide and its derivative globotriaosylsphingosine in the lysosomes of cells in various tissues (vascular endothelium, kidneys, heart, central nervous system, peripheral nervous system, etc.), as well as in bodily fluids [1].

These changes result in multisystem manifestations of the disease, leading to progressive organ damage and, consequently, a reduced quality and length of life. In the absence of appropriate treatment, death can occur at the age of 40-50 years due to cardiovascular, cerebrovascular complications, and renal failure.

At the same time, this diagnosis is not always established in a timely manner, leading to late diagnosis and the absence of pathogenetic therapy. Considering the large volume of available information and the numerous contentious issues surrounding FD, there is a need to analyze the literature data.

Objective—To summarize current data regarding the mechanisms of disease onset, clinical manifestations, diagnostic criteria, features of the course, and treatment of FD based on studies conducted in recent years.

Materials and methods

This review article utilized the work of Russian and foreign authors and involved a systematic search in the PubMed and e-library databases, on internet platforms, and in print sources using the following keywords: "Fabry disease," "alpha-galactosidase A," "lysosomal storage disease," "Globotriaosylceramide," "Anderson-Fabry disease," "diffuse angiokeratoma of the trunk" for the period from January 1, 2015, to January 1, 2026. Based on the search results, consensus documents, meta-analyses, scientific articles, and clinical cases were analyzed. Materials, studies, or articles that did not meet quality standards were excluded.

Results

Epidemiology. In terms of prevalence, FD ranks second among LSDs after Gaucher disease. Prevalence rates vary widely and are directly dependent on the disease phenotype. Foreign authors report the following rates for patients with the classic phenotype: from 1 in 117,000 to 1 in 476,000 in the general population [2]. Moreover, a predominance in prevalence is observed in males: 1 in 40,000 and 1 in 60,000 [3]. Considering the late-onset phenotypes, a higher actual prevalence of this pathology is clearly suggested. For example, according to a European multicenter study conducted by Elliott et al., pathogenic galactosidase mutations were identified in 0.5% of 1,386 patients with hypertrophic cardiomyopathy (HCM). According to Petrukhina A.A. et al., as of 2024, 230 clinical cases of FD were registered in Russia [4]. In another study by Eng C.M., Germain D.P., et al., the frequency of pathogenic mutations during screening was 1% [5]. Furthermore, interesting data emerged from screening studies in Italy, where the frequency of GLA gene mutations reached 1 case per 8,800 newborns [6]. In Taiwan, a similar study identified 1 case per 1,600 newborn males. It has been established that the average age of diagnosis for men and women is 24 and 31 years, respectively. At the same time, undiagnosed or untreated typical FD can reduce life expectancy by 15 years in men and 20 years in women [7].

Literature data were analyzed regarding the frequency of FD in various conditions. Thus, FD was found in 4.2% of men and 2.15% of women with early stroke, in 0.9% and 3.9% of men and women with HCM of unknown origin, and in 0.33% and 0.10% of men and women with end-stage renal disease, respectively [8].

Classification of the disease. Two forms of the disease are distinguished: the classic, or typical form, and the non-classic form, also known as the late-onset form [4, 8].

In the first case, patients with the classic phenotype may exhibit signs and symptoms of FD from early childhood, which are polyorganic in nature. These signs include neuropathic pain, verticillata cornea, gastrointestinal symptoms, hypohidrosis, and angiokeratoma. Delayed manifestations of the disease include chronic kidney disease (CKD) with renal failure, HCM, cardiac rhythm and conduction disturbances, hearing loss (bradyacusia or hypoacusia), and cerebrovascular accidents. This variant is characterized by the absence or significant reduction (less than 3% of the expected value) of α-Gal A activity.

In the second variant, signs and symptoms of FD develop at a later age, representing a milder course of the disease. Simultaneous involvement of all the aforementioned target organs may be insignificant or absent altogether, but there is often predominant and typically severe involvement of a single organ. In the non-classic variant, FD more frequently affects the brain, heart, or kidneys. This variant is characterized by a less significant reduction in α-Gal A levels. However, cardiac involvement is one of the most common clinical manifestations in patients with both variants of FD.

Clinical Manifestations of Fabry Disease

FD is "multifaceted" and presents with diverse manifestations even among members of the same family, meaning the clinical picture ranges from a complete absence of symptoms or a mild form to a severe one (Fig. 1). The spectrum of possible complaints is quite varied and depends on several factors, such as the disease form, individual characteristics of the disease course, gender, etc.

The disease is progressive in nature, and, as a rule, without specific treatment, death occurs in the 4th-5th decade of life due to renal failure or cardiovascular complications [9].

Cardiovascular Manifestations. It has been established that myocardial damage is a prognostically unfavorable and frequent manifestation of FD [11]. According to statistics, cardiac involvement is the leading cause of death in 34% of men and 57% of women [8, 11]. The mechanisms of cardiovascular system damage result from the deposition of glycosphingolipids in cardiomyocytes, endothelial and smooth muscle cells of vessels, endocardial cells, conducting tissue, and valvular fibroblasts. This leads to the formation of left ventricular hypertrophy (LVH), diastolic dysfunction, myocardial ischemia, and the occurrence of cardiac rhythm and conduction disturbances [8, 12].

According to research data, screening for FD among over 5,400 patients with LVH and/or HCM of unclear etiology revealed a frequency of pathogenic mutations of 0.93% and 0.90%, respectively [13]. Other manifestations of this disease are rhythm and conduction disturbances. Manifestation of coronary

DOI: 10.24412/2311-1623-2026-50-57-65

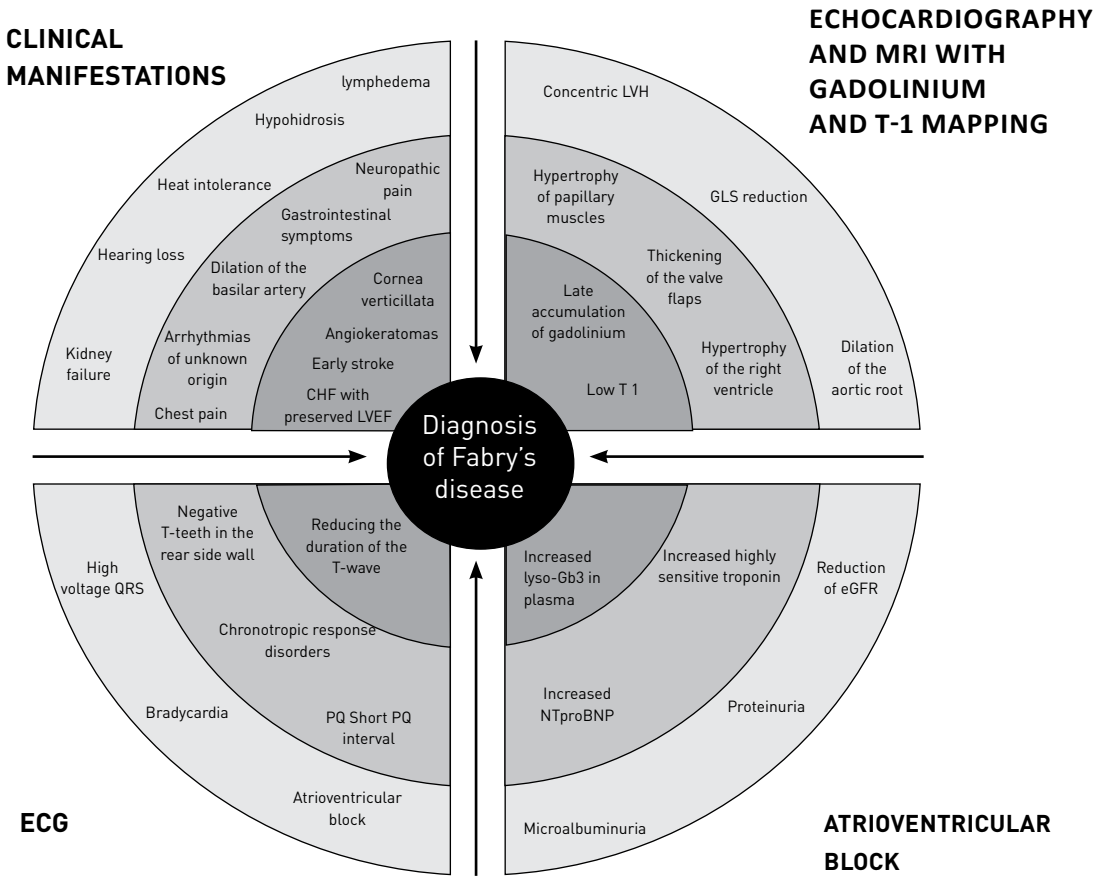

Fig. 1. Clinical manifestations and results of laboratory and instrumental studies that may indicate FD [10]. Darker shading indicates more characteristic signs of the disease

artery disease in the form of myocardial infarction occurs in 2% of patients with FD, while angina pectoris occurs in 13–20% of patients, often in combination with LVH [8, 13]. Valve involvement is also frequently observed in FD but has no particular clinical significance. As mentioned above, in the non-classical form with monosymptomatic course, cardiac involvement may be the sole manifestation of FD.

Renal involvement. Kidney damage can occur either as an isolated manifestation in the non-classic variant of FD or in conjunction with other syndromes in the classic variant. Renal involvement most often develops during adolescence and manifests as a nephritic urinary syndrome, potentially progressing to nephrotic syndrome and declining renal function up to end-stage chronic renal failure (CRF), which is one of the leading causes of death in patients [14].

Gastrointestinal manifestations. Clinical manifestations of GI tract involvement include non-specific symptoms such as decreased appetite, weight loss, intermittent cramping abdominal pain, bloating, unstable stools, nausea, and vomiting. The onset of gastroenterological manifestations of FD is more often observed in childhood and adolescence [8, 15].

Nervous system involvement. Damage to both the peripheral and central nervous systems is possible. Polyneuropathies, resulting from peripheral nervous system damage, are relatively common clinical syndromes in FD. They occur in 60–80% of patients, manifesting as chronically severe, sometimes debilitating neuropathic pain in the extremities, presenting as acroparesthesias, allodynia, and hyperpathia. Characteristic types of chronic pain include burning, shooting, and stabbing. The pathogenesis of neuropathy involves two mechanisms of neuropathic pain: central and peripheral. In the first case, damage to the thalamus occurs due to calcification in FD. In the formation of peripheral neuropathic pain, accumulation of globotriaosylceramide occurs in nerve axons, dorsal root ganglia, and vasa nervorum. Central nervous system involvement manifests as vascular events such as transient ischemic attacks, ischemic or hemor-rhagic stroke occurring between the ages of 20 and 50. Stroke can be a form of monosymptom-

atic manifestation of the atypical form of FD. The prevalence of stroke is about 6.9% and 4.3% in men and women, respectively. Chronic cerebral ischemia can lead to vascular dementia, including memory decline, impaired concentration, and behavioral disturbances [8, 16].

Sweating disorders. Accumulation of globotriaosylceramide in sweat glands, vessels, and autonomic nerve fibers leads to hypohidrosis or anhidrosis in the majority of cases.

Lymphatic system involvement. In some cases, lymphedema (pathological accumulation of protein-rich fluid in the interstitial space due to impaired lymph transport, accompanied by an increase in the volume of the affected organ) may be observed. Lymphedema can result from congenital or acquired impairment of lymph transport through lymphatic vessels due to glycolipid deposition in the lymphatic vessel walls [8, 17]. Scientific literature describes cases of lymphedema complicated by trophic disorders, leading to ulceration of the skin.

Otorhinolaryngological manifestations. Involvement of the auditory and vestibular systems may manifest as tinnitus (unilateral or bilateral), sensorineural hearing loss, and dizziness [8, 18].

Skin manifestations. Angiokeratomas are a manifestation of skin involvement in patients with FD. These are well-demarcated papules, red, dark red, burgundy, purple, or blue-black in color, ranging from 0.2 to 1.0 cm in size, predominantly located symmetrically in the groin area, on the buttocks, thighs, around the navel, and on the palms. Initially, angiokeratomas appear in childhood, are lighter, flatter, and more compressible, but with age their number and size increase, and they become darker, harder, and more elevated above the skin surface. Cases of angiectasias in the oral mucosa and conjunctiva have been described. Skin manifestations are not obligatory clinical signs.

Ophthalmological manifestations. Lens and corneal involvement occurs in more than 50% of patients with FD. A typical symptom is corneal opacity in a whorl-like pattern (in 70–90% of patients). Occasionally, lens opacities such as posterior radial subcapsular cataract, the so-called "Fabry cataract," and bilateral anterior capsular and subcapsular cataracts may occur, but these are not pathognomonic signs [19].

External features. External signs resemble those of acromegaly—prominent supraorbital ridges and frontal bosses, a protruding lower jaw, thickened lips, and a depressed nasal bridge are often observed in hemizygous males.

Features of the clinical picture in childhood and adolescence. Most symptoms of FD manifest during adolescence and young adulthood; however, verifying the diagnosis of FD in children is difficult due to the non-specific nature of the disease syndromes. For example, GI manifestations in this disease can only serve as an indirect marker due to their low specificity. Angiokeratomas in childhood are often solitary and may occur in atypical locations such as the chest, oral mucosa, and ears.

Manifestations of cardiovascular system involvement are also non-specific, presenting as periodic non-significant decreases and/or increases in blood pressure, asymptomatic or oligosymptomatic arrhythmias mimicking autonomic dysfunction. Timely diagnosis of renal involvement in FD is challenging, as this condition may manifest only as transient microalbuminuria [8, 20]. Rarer, less specific manifestations of FD in this age group include glossitis, granulomatous cheilitis, osteopenia, osteoporosis, hypothyroidism, thickening of the terminal phalanges, anemia, and respiratory disorders.

Diagnosis of the disease. In establishing a diagnosis of FD, medical history data and clinical-laboratory (molecular-genetic and biochemical) research methods are important. Verification of the classic variant of FD relies on the combination of multi-organ involvement, while verification of atypical variants is possible through screening of risk groups. It is important to note that FD should be suspected in all patients with young-onset stroke and LVH of unknown etiology.

Laboratory diagnostic tests

1. **Enzyme assay:** Determination of alpha-galactosidase A (AGAL) activity in dried blood spots on filter paper or in blood leukocytes for all male and female patients; however, in about one-third of female patients with FD, this indicator may be within the normal range.

2. **Identification of mutations** in the gene encoding AGAL for men with reduced enzyme activity and for women with clinical signs of FD using Sanger sequencing of all exons and flanking intronic regions.

DOI: 10.24412/2311-1623-2026-50-57-65

This method is also necessary for identifying the familial GLA gene mutation in relatives of the proband for prenatal and preimplantation diagnosis, as well as for identifying heterozygous female carriers of FD.

3. **Quantitative determination** of globotriaosylsphingosine in dried blood spots or blood plasma is performed for all patients, both for biochemical confirmation of the FD diagnosis and for biochemical monitoring of therapy, given that this metabolite does not reach normal values in patients with FD.

4. Conducting laboratory tests according to clinical guidelines for managing patients with CRF (at least once every 6 months) and HCM when clinical signs of renal and cardiac involvement are present.

5. For all patients, regular (at least once every 6 months) determination of protein and albumin levels in urine and estimation of glomerular filtration rate are recommended to detect renal pathology.

6. Biopsy and pathological examination of kidney and heart tissues are recommended only in complex differential diagnostic cases [8, 21].

Instrumental diagnostic tests

To detect LVH, electrocardiography, echocardiography and Doppler echocardiography, and MRI are indicated. MRI of the brain is also recommended to detect possible involvement of the cerebral white matter (leukoaraiosis), gray matter (calcification of the posterior thalamus), ischemic foci, intracerebral hematomas, and vascular malformations. Additionally, tonal audiometry every 3 years is recommended to detect hearing loss.

The patient's examination plan also includes consultations with a cardiologist (at least once every 6 months) and an ophthalmologist (at least once every 3 years) [8].

Treatment principles

Treatment includes pathogenetic, symptomatic, and surgical approaches. Pathogenetic therapy includes enzyme replacement therapy and chaperone therapy. Other treatment methods are under clinical trial development, such as substrate reduction therapy, other enzyme replacement agents, and gene therapy.

Pathogenetic therapy. Pathogenetic therapy includes enzyme replacement therapy, which is currently represented by two drugs on the Russian pharmaceutical market: agalsidase alfa and agalsidase beta. The efficacy of therapy was evaluated in over 48 prospective studies, which showed a positive treatment effect, including reduced myocardial mass, decreased Cb3 levels in kidney tissues, reduced neuropathic pain, improved hearing, and enhanced quality of life. The use of a chaperone (migalastat), which is currently not registered in the Russian Federation, is also being considered. New treatment options for substrate-reducing therapy include lucerastat and venglustat, which are in Phase 2-3 trials. New pegylated forms of α-Gal A (pegunigalsidase alfa) and gene therapy agents are also being developed [9, 22]. The success of therapy directly depends on the disease form, timing of treatment initiation, drug dosage, potential development of antibodies to drug components, and several other factors.

Symptomatic therapy. Symptomatic therapy includes pain management and treatment of multisystem pathology according to current clinical guidelines. Symptomatic therapy may be prescribed by a medical commission decision [23]. For example, for pain management, the use of analgesics is recommended, along with eliminating or limiting provoking factors such as intense physical activity, temperature fluctuations (cold and/or hot weather), etc. For patients with cardiovascular complications, antiplatelet agents, anticoagulant, antiarrhythmic, and antihypertensive therapy are recommended. For patients developing gastrointestinal complications, the use of proton pump inhibitors or H_2-histamine receptor blockers is permitted. In the presence of proteinuria and arterial hypertension syndrome, the addition of angiotensin-converting enzyme inhibitors or angiotensin II blockers is recommended for nephroprotective purposes.

Surgical treatment. In cases of end-stage renal failure, hemodialysis and/or kidney transplantation are necessary according to standards and clinical guidelines for managing this pathology.

For patients with atrioventricular block, pacemaker implantation is performed according to applicable clinical standards and recommendations, and for life-threatening arrhythmias, implantable cardioverter-defibrillator implantation is performed, respectively [8, 24]. For skin manifestations, removal of angiokeratomas is recommended in consultation with the patient.

Conclusion

The results of the literature analysis indicate that in recent years, due to a deeper understanding of this pathology, diagnostic algorithms have been significantly improved, including genetic screening of patients' family members, and new methods of pathogenetic treatment for FD have been introduced. However, problems of late diagnosis of FD and, consequently, late initiation of specific therapy persist, which affects the prognosis and quality of life of patients. Further in-depth study of the complex issues of disease pathophysiology will allow for the improvement and enhancement of diagnostic and treatment stages for this pathology and, accordingly, optimize the individualized approach to managing this category of patients in real clinical practice.

Conflict of interest: none declared.

References

1. Sakuraba H, Togawa T, Tsukimura T et al. Plasma lyso-Gb3: a biomarker for monitoring Fabry patients during enzyme replacement therapy. ClinExpNephrol. 2018. 22(4): 843-9. DOI: 10.1007/s10157-017-1525-3
2. Polo G, Burlina A, Ranieri E et al. Plasma and dried blood spot lysosphingolipids for the diagnosis of different sphingolipidoses: a comparative study. Clinical Chemistry and Laboratory Medicine (CCLM). 2019;57(12)1863-74. DOI: 10.1515/cclm-2018-1301
3. Chung-Lieh Hung et al 2024 Update of the TSOC Expert Consensus of Fabry Disease, Acta Cardiol Sin 2024;40:544 568; DOI: 10.6515/ACS.202409_40(5).20240731A
4. Petrukhina AA, Nasonova SN, Zhirov IV et al. The difficulties of diagnosing Fabry's disease in real clinical practice. Acta Biomedica Scientifica. 2025; 10(1):50-58. Russian. DOI: 10.29413/ABS.2025-10.1.5
5. Ortiz A, Germain DP, Desnick RJ et al. Fabry disease revisited: Management and treatment recommendations for adult patients. Molecular Genetics and Metabolism. 2018. 123(4): 416-27. DOI: 10.1016/j.ymgme.2018.02.014
6. Limongelli G, Monda E, Tramonte S, et al. Prevalence and clinical significance of red flags in patients with hypertrophic cardiomyopathy. Int J Cardiol. 2020;299:186-91. DOI: 10.1016/j.ijcard.2019.06.073
7. Körver S. Development and clinical consequences of white matter lesions in Fabry disease: a systematic review. Molecular genetics and metabolism. 2018. 125(3): 205-216. DOI: 10.1016/j.ymgme.2018.08.014
8. Fabry's disease: clinical recommendations / Association of Medical Geneticists; Union of Pediatricians of Russia.2019. 53 p. Russian.
9. Spada M, Baron R, Elliott PM et al. The effect of enzyme replacement therapy on clinical outcomes in paediatric patients with Fabry disease—A systematic literature review by a European panel of experts.Mol Genet Metab. 2019. 126(3): 212-23. DOI: 10.1016/j.ymgme.2018.04.007
10. Pieroni M, Moon JC, Arbustini E, et al. Cardiac involvement in Fabry disease. J Am CollCardiol. 2021;77:922–33. DOI: 10.1016/j.jacc.2020.12.024
11. Germain DP, Arad M, Burlina A et al. The effect of enzyme replacement therapy on clinical outcomes in female patients with Fabry disease—A systematic literature review by a European panel of experts. Mol Genet Met ab. 2018. 126(3): 224-35. DOI: 10.1016/j.ymgmr.2019.100454
12. Moiseev SV, Tao EA, Moiseev AS et al. Clinical manifestations and outcomes of Fabry's disease in 150 adult patients. Clinical pharmacology and therapy.2021;30(3):43-51. Russian. DOI: 10.32756/0869-5490-2021-3-43-51
13. Rushkevich YuN, Trukhanova IS, Likhachev SA et al. Fabry's disease: literature review, own clinical observation. «Neurology and Neurosurgery Eastern Europe»,2024;14(1):59-73. Russian DOI: 10.34883/PI.2024.14.1.046
14. Tao EA, Moiseev AS, Novikov PI et al. The effectiveness of family screening for Fabry's disease in the Russian population. Clinical pharmacology and therapy. 2020;29(2):34-39. Russian. DOI: 10.32756/0869-5490-2020-2-34-39
15. Germain DP, Elliott PM, Falissard B et al. The effect of enzyme replacement therapy on clinical outcomes in male patients with Fabry disease: A systematic literature review by a European panel of experts. Mol Genet Metab Rep. 2019. 19: 100454. DOI: 10.1016/j.ymgmr.2019.100454
16. El Sayed M, Postema PG, Datema M,et al. ECG changes during adult life in Fabry disease: results from a large longitudinal cohort study. Diagnostics 2023;13:354. DOI: 10.3390/diagnostics13030354
17. Tao EA, Moiseev AS, Bulanov NM et al. Chronic renal failure in Fabry's disease: over all survival with the use of various methods of renal replacement therapy. Clinical pharmacology and therapy.2023;32(4):58-63.Russian. DOI: 10.32756/0869-5490-2023-4-58-63
18. Lenders M, Nordbeck P, Kurschat C, et al. Treatment of Fabry disease management with migalastat -outcome from a pro spective 24 months observational multicentre study (FAMOUS).

Eur Heart J Cardiovasc Pharmacother 2022;8:272-81. DOI: 10.1093/ehjcvp/pvab025

19. Camporeale A, Bandera F, Pieroni M, et al. Effect of Migalastat on cArdiac InvOlvement in FabRry DiseAse: MAIORA study. J MedGenet2023;60:850-8. DOI: 10.1136/jmg-2022-108768
20. Izhar R, Borriello M, La Russa A, et al. Fabry disease in women: genetic basis, available biomarkers, and clinical manifestations. Genes (Basel) 2023;15:37. DOI: 10.3390/genes15010037
21. Moiseev AS, Mershina EA, Safarova AF et al. Heart damage in Fabry disease: features of the course and diagnostic value of magnetic resonance imaging and speckle-tracking echocardiography. Clinical pharmacology and therapy.2022;31(3):22-29. Russian. DOI: 10.32756/ 0869-5490-2022-3-22-29
22. Moiseev SV, Tao EA, Moiseev AS et al. Fabry's disease as a cause of hypertrophic cardiomyopathy. Clinical pharmacology and therapy. 2023;32(1):36-41. Russian. DOI: 10.32756/0869-5490-2023-1-36-41
23. Nowicki M, Bazan-Socha S, Blazejewska-Hyzorek B, et al. A re view and recommendations for oral chaperone therapy in adult patients with Fabry disease. Orphan et J Rare Dis 2024;19:16. DOI: 10.1186/s13023-024-03028-w
24. Tao EA, Moiseev AS, Bulanov NM et al. Clinical phenotypes of Fabry's disease in adult patients. Clinical pharmacology and therapy.2024; 33(2):56-62. Russian. DOI 10.32756/ 0869-5490-2024-2-56-62

International Heart and Vascular Disease Journal. Volume 14, № 50, June 2026
ISSN: 2311-1623 (Print)
ISSN: 2311-1631 (Online)
http://www.heart-vdj.com

Author Guidelines

Manuscript publication rules

in the International heart and vascular disease journal

Edit from December, 2021

Disclaimer: The rules came into effect from December 2021. The rules describe the conditions of publication of manuscripts (articles) through the site http://www.heart-vdj.com. The editorial Board is ready to answer questions and help authors by e-mail: submissions.ihvdj@gmail.com.

The *International heart and vascular disease journal* has been published since 2013. It is official journal of the Cardioprogress Foundation. The target audience of this peer-reviewed journal is cardiologists and internal disease specialists. The journal is primarily focused on questions of epidemiology, prevention, and cardiac pharmacotherapy. It also publishes lectures and literature reviews on various problems of modern cardiology, reports on new diagnostic methods, and other information which is important for the practitioners.

The General criteria for the publication of articles in the International heart and vascular disease journal are the relevance, novelty of the material and its value in theoretical and/or applied aspects.

The languages of publications are Russian and English. Journal is peer-reviewed, with multistage editing. Editorial board is presented by the leading cardiologists from different countries and Russia.

International heart and vascular disease journal aims to ensure that its publications fulfill the requirements of international publishing standards, such as the Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication, by the International Committee of Medical Journal Editors, ICMJE (http://www.icmje.org), and the recommendations by the Committee on Publication Ethics, COPE (http://www.publicationethics.org.uk).

All clinical trials should be performed and described in full accordance with the CONSORT standards (http://www.consort-statement.org), observational research — STROBE (http://www.strobe-statement.org), systematic reviews and meta-analyses — PRISMA (http://www.prisma-statement.org), diagnostic accuracy — STAR (http://www.stard-statement.org).

I. The International heart and vascular disease journal accepts the following manuscripts:

1) *Original papers* present the results of clinical studies. The word limit is 3.000 (including references, tables, and figure legends). The maximal number of references is 15. The structured abstract should contain 5 sections (**Aim, Material and Methods, Results, Conclusion**, and **Key words**), and be no longer than 300 words.

2) *Lectures*, or clinically oriented reviews, are written by experts in broader areas of medicine. Lectures could be focused on epidemiology, pathophysiology, diagnostics, treatment, and prevention. The word limit is 5.000 (including references, tables, and figure legends). The maximal reference number is 80. The unstructured abstract is no longer than 150 words.

3) *Literature reviews* are focused on more specific topics, compared to lectures. The word limit is 4.500 (including references, tables, and figure legends). The maximal reference number is 50. The unstructured abstract is up to 150 words.

4) *Clinical case* is a brief report on a complex diagnostic problem and its solution, or a description of

a rare clinical observation. The word limit is 600 (including references, tables, and figure legends). The maximal number of references is 5. No abstract is required.

5) *Clinical opinion* informs the readers on the topics of cardiovascular medicine and related disciplines. The word limit is 2.500 (including references, tables, and figure legends). The maximal number of references is 15.

The journal accepts for publication original phase 2, 3 and 4 clinical studies. Literature reviews should be based on sources not older than 5 years.

II. Information about the article, which includes the following sections, is combined into a single file "letter (cover)":

1) the manuscript is not under consideration in another edition has not been previously published contains a full disclosure of the conflict of interest all authors meet the criteria of authorship, it was read and approved the author (s) are responsible for the power of attorney submitted in the manuscript materials. 6) all contact information of the author responsible for correspondence information about previous publications of the authors on the same topic or pre-publication.

If the manuscript is a part of the thesis, it is necessary **to specify** the estimated terms of thesis defense.

The "letter of direction (accompanying)" should be made out on one or two sheets. Using the form of the official institution-at the choice of the author's team. In the address: "to The chief editor of the Russian cardiology journal, academician of RAS, Professor Oganov R. G.". The signatures of **all authors** should be placed at the bottom.

"Directional (cover) letter" is scanned. File format. jpeg attached as an additional file of the manuscript.

The absence of a letter or incomplete text of the letter (not containing the above items) is the basis for refusal to accept the manuscript for consideration.

III. Registration on the Website and information about the authors.

Any of the authors can submit an article to the journal. Usually it is the one who then conducts correspondence with the editorial office and to whose mail notification letters come (when submitting a manuscript through the site, you can choose to send notifications to all authors).

The author registers on the site, entering his full name. In the form to be filled in when submitting an article, all authors and all additional information (places of work, positions, academic titles, institutions, ORCID — all authors) are indicated.

If the author has several places of work, it is written: 1. "The name of the institution..." 2. "Name of institution."... The name of the institution is written in abbreviated form, for example, Moscow state University, Moscow. Brackets are not put.

How to fill in the article metadata: all data that is entered in the "article metadata" must exactly match the data specified in the text of the article!

Authors ' names (you can not write in full, the format of the journal provides for the publication of names and initials. Therefore, in the "Windows", where the name and patronymic of the authors are written in capital letters with a dot (example: A.).

Names of institutions (write the official name. At the same time — there is a reduction of Federal, STATE, etc.; the quotation marks are placed; Ministry of health of Russia, a city without the letter G.

Positions and titles (using traditional abbreviations: PhD, senior researcher, leading researcher, PhD, C.b.N., MD), head reduces to the head., then write the full name of the laboratory/Department / Department; Director, head, Professor — is not reduced.

The order of the authors. Authors ' priority should be entered into the system in accordance with the order of the article. The movements are made by small arrows "top" / "bottom", which are located under the data of each of the authors. The data of the author responsible for the correspondence, put a dot in a circle denoting this information. Other authors point do not put.

Summary. Sections of the abstract should exactly match the sections prescribed In the rules for authors. If the sections are not correct, the Editors will ask to correct them. What the authors are currently publishing on the site will then be included in all systems after the final publication. Be careful!

Making literary references. Submitted article will not be reviewed until the correction of literary references in accordance with the rules for authors is made. The authors "forget" and somewhere to remove point (such inconsistencies can be corrected in the Revision), but if the design literature is radically different from what is required or present hyperlinks,

the Editors will not start with the article to eliminate errors.

Keyword. They are written with a small letter, separated by a semicolon. At the end put a point. In the text of the article the keywords are written separated by commas.

A file is prepared separately in Word, which is then sent as an additional file. The file must contain:

Title page of the manuscript. The title of the manuscript is written in capital letters, without hyphenation, in bold. Initials and surnames of authors-Ivanov I. I., Petrov P. p. the full name of organization (s) from which (s) there was a manuscript, the city, the country is Given. Footnotes are in Arabic numerals after the authors ' names and before the names of institutions.

Example of design:

THE PREVALENCE OF RISK FACTORS OF NONCOMMUNICABLE DISEASES IN THE RUSSIAN POPULATION IN 2012 — 2013. THE RESEARCH RESULTS OF THE ESSE-RF

Muromtseva G.A.[1], Kontsevaya A.V.[1], Konstantinov V.V. [1], Artamonova G.V. [2], Galaganova T.M. [3],...

[1] FGBU State research center of preventive medicine of the Ministry of health of Russia, Moscow;

[2] FGBU Research Institute of complex problems of cardiovascular diseases SB RAMS, Kemerovo;

[3] RD VPO North Ossetian state medical Academy, Vladikavkaz;..., Russia.

Information about the authors, where indicated: full name, place of work of all authors, their positions, ORCID; full contact information is required for one (or more) of the author and includes e-mail, available phone number.

All members of the group of authors should meet all four criteria of authorship set forth in the ICMJE recommendations: 1) concept and design development or data analysis and interpretation, and 2) manuscript justification or verification of critical intellectual content, and 3) final approval for publication of the manuscript, and 4) consent to be responsible for all aspects of the work, and assume that issues relating to the thoroughness and diligent execution of any part of the study submitted are duly investigated and resolved. This information should also be contained in the document.

If the submitted material has authors who do not meet the criteria of authorship, but have made some contribution to the work, they should be listed in this document and at the end of the article in the section of Acknowledgements.

Information on conflict of interest / funding.

The section contains the disclosure by all authors of possible relations with industrial and financial organizations that may lead to a conflict of interest in connection with the material presented in the manuscript. It is desirable to list the sources of funding for the work. If there is no conflict of interest, it is written: "Conflict of interest is not declared." Information on the existence of a conflict of interest should also be reflected in the Conflict of interest section at the end of the article.

Information about grants. Should be mentioned at the end of the article in the section Acknowledgements and at the end of the section Material and methods — with a full description of the role of the source of funding in the performance of work (design, information collection, analysis, data interpretation, etc.).

Information and ethics in the study.

Example of design:

The study was carried out in accordance with the standards of good clinical Practice (Good Clinical Practice) and the principles of the Helsinki Declaration. The study Protocol was approved by the Ethical committees of all participating clinical centers. Prior to being included in the study, written informed consent was obtained from all participants.

This information should also be reflected in the Material and methods section of the article.

All additional information (permits, questionnaires, etc.) can be requested from the authors in addition to the preparation of the work for printing.

Information on overlapping publications (if available).

Copyright. The use of any material (tables, figures) marked with a copyright icon in the article should be confirmed by a special permission from the author or publisher.

Information about the obtained consent in patients for the study.

Obtaining consent from patients for the study should also be reflected in the Material and methods.

For all clinical trials: information about the registration and placement of data on the study in any public register of clinical trials. The term "clinical study" refers to any research project that affects people (or groups of subjects) with/or without a comparative control group, studies the interaction between inter-

ventions to improve health or the results obtained. The world health organization offers the primary register: International Clinical Trials Registry Platform (ICTRP) (www.who.int/ictrp/network/primary/en/index.html). The clinical study is considered to be reliable in a group of more than 20 patients.

The number of words in the article (excluding summaries, sources of literature, figure captions and tables), the number of tables and figures.

The absence of an information file or incomplete text (not containing the above items) is the basis for refusal to accept the manuscript for consideration.

IV. Manusctipt submision check-list

Since the main file of the manuscript is automatically sent to the reviewer for» blind review», it should not contain the names of the authors and institutions. The file contains only the following sections:

Article title
Summary with key words
List of abbreviations
Text
Acknowledgements (if any)
List of references
Tables, figures (if they can be embedded in the text of Word format).

The article title is written in capital letters (PREVALENCE of RISK FACTORS...), the end point is not needed. The title should clearly reflect the purpose of the work.

Summary with key words-sections are drawn up each with a separate line, highlighted in bold. The abstract should contain only those sections that are described in the rules for authors. For example, there is no section "Relevance" in the summary. The authors prescribe the relevance of their work in the introductory section of the manuscript.

List of abbreviations — when compiling a list of abbreviations to the article, including text, tables and figures, only those used by the author 3 or more times are included. Usually shrink often used in manuscripts of the terms (e.g., hypertension, CHF FC) and title of clinical trials (SOLVD, TIMI, HOPE).

The first reference to an abbreviation is always accompanied by the full spelling of the abbreviated concept, and the abbreviation is indicated in brackets. For example, blood pressure (BP); heart rate (HR). Capital letters are more often used to denote abbreviations. If abbreviations are used only in tables and figures, and are not used in the text, they should not be included in the list of abbreviations, but should be given a transcript in the note to the table or figure. The summary of the article, as a separate document, is subject to the same rules as the article (abbreviations are made when they are used 3 or more times).

Abbreviations should be generally accepted and understandable to the reader, in accordance with the generally accepted norms in the scientific literature. Undesirable abbreviations that coincide in writing with others that have a different meaning.

Abbreviations in the list of abbreviations are written in alphabetical order, separated by commas, in solid text, using "dash". **Example of design:** BP-blood pressure, HR-heart rate.

Text — the text of the manuscript of the original works should be structured: Introduction, Material and methods, Results, Discussion and Conclusion. The text of reviews and lectures can be unstructured.

Text is printed on A4 sheet, font size — 12 pt, line spacing — 1.5, margins 2 cm on all sides. The system of SI units is used for processing the material, the% sign is put through a space from the number, the value of p is written with a semicolon: $p < 0.0001$; the value of n is written with a small letter (n=20); signs >, <, ±, =, +, — when numerical values are written without a space; the value of "year" or "year" is issued — 2014 or 2002 — 2014.

The article should be carefully verified by the author (s). The authors are responsible for the correctness of citation, doses and other factual materials.

Introduction — it is necessary to describe the context and prerequisites of the work (what is the essence of the problem and its significance). It sets certain goals or describes the object of the study, or a hypothesis that needs to be tested by comparison or observation. Only those sources that directly indicate the problem are cited.

Statistics — all published materials are reviewed by an expert in statistics and must meet "Uniform requirements for manuscripts submitted to biomedical journals" (Uniform Requirements for Manuscripts Submitted to Biomedical Journals, Ann Intern Med 1997, 126: 36 — 47). In the preparation of the statistical part of the work it is recommended to use special guidelines, for example, the European journal of cardiology: www.oxfordjournals.org/our_journals/eurheartj/for_authors/stat_guide.html

Statistical methods are described in detail in the Material and methods section.

Acknowledgements — all participants who do not meet the authorship criteria should be listed in the Acknowledgements section, which is located at the end of the article before the Literature section.

Making graphs, diagrams and drawings — tables and figures should provide the reader with visual information, be interesting and educational. They should be placed after the text of the article, as the reviewer and editor look at the manuscript as a whole. However, to print in the journal (at the stage of creating a layout) graphics, diagrams and drawings are required in electronic form in the formats "MS Excel", "Adobe Illustrator", "Corel Draw", "MS PowerPoint", photos with a resolution of at least 300 dpi.

The names of the graphs and figures, as well as notes to them should be placed under the figure/graph or placed at the end of the article.

These files are referred to as additional files. Figures should not repeat the materials of the tables.

Tables should contain the compressed, necessary data. Each table is placed at the end of the text (after the list of references) with the number, name and explanation (note, abbreviations).

The tables should clearly indicate the dimension of the indicators and the form of data (M±m; M±SD; Me; Mo; percentiles, etc.). All figures, totals and percentages should be carefully verified, and also correspond to the mention in the text. The explanatory notes are given below the table, if necessary. The footnotes must be in the following order: *, †, §, ||, ¶, #, **, †† etc.

Abbreviations should be listed in a footnote below the table in alphabetical order (for tables its list of abbreviations!).

Each first mention of a figure or table in the text is highlighted with a yellow marker. If a reference to a figure or table is included in the sentence, the full spelling of the word «figure 1», «table 1» is used; if the words are enclosed in brackets, the abbreviation is used (Fig. 1), (table. 1).

Providing the main file of the manuscript with the names of the authors or institutions is the basis for refusal to accept the manuscript for consideration.

V. The list of references.

In the form to fill in when submitting the article provides a list of cited literature (section — Literature).

Literary references are listed in the order of citation in the manuscript. The text refers to the serial number of the cited work in square brackets [1] or [1, 2]. Each link in the list is on a new line. All documents referred to in the text should be included in the list of references.

References to works that are not in the list of references and Vice versa, references to unpublished works, as well as to works of many years ago (>10 years) are not allowed. The only exceptions are rare highly informative works. Especially close attention to this item, please pay to those authors who submit "literature Review".

The bibliographic description contains the names of the authors up to three, after which, for domestic publications should indicate "et al.", for foreign — "et al." When citing articles from journals indicate in the following order the output: the name and initials of the authors, the name of the source, year, volume, number, pages (from and to). When citing articles from the collections indicate the output: name, initials, title, title of the collection, place of publication, year of publication, page (from and to).

If you want to make a quotation of the authors ' names in the text, you must specify the name of the first author with the initials, the year of work. Example design: Smith AA, et al. (2018).

With the purpose of increase of citation in the journal is the transliteration of Russian sources with the use of the official languages in the following order: the authors and the journal title is transliterated in the Latin alphabet, and the name of the article is semantic transliteration (translation into English). The name of the source where the work is published is transliterated in Latin if the source (journal) does not have an official name in English).

All Russian-language sources of literature should be presented in the transliterated version of the model given below.

The author (s) are responsible for the correctness of the data given in the references.

The list of references should correspond to the format recommended by the American National organization For information standards (national Information Standards organization — NISO), adopted by the National Library of Medicine (NLM) for databases (Library's MEDLINE/PubMed database) NLM: http://www.nlm.nih.gov/citingmedicine Oh? The names of periodicals may be abbreviated. Usually

this form of writing is accepted by the publisher; it can be found on the website of the publisher, or in the list of abbreviations Index Medicus.

Mandatory all articles DOI specified, all books ISBN. References to dissertations, patents, theses and any collections without output and ISBN are not accepted.

Examples of link design:

Article citation:

Smith A, Jones B, Clements S. Clinical translation of tissue-engineered airway. Lancet. 2008;372:1201 — 09. DOI:10.00000/0000-0000-.

Russian-language sources with transliteration:

Bart BYa, Larina VN, Brodskyi MS, et al. Cardiac remodelling and clinical prognosis in patient with chronic heart failure and complete left bundle branch block. Russ J Cardiol. 2011;6:4 — 8. Russian. Барт Б. Я., Ларина В. Н., Бродский М. С., и др. Ремоделирование сердца и прогноз больных с хронической сердечной недостаточностью при наличии полной блокады левой ножки пучка Гиса. Российский кардиологический журнал. 2011;6:4 — 8. DOI:10.15829/1560-4071-2011-6-4-8.

Book:

Shlyakhto EV, Konradi AO, Tsyrlin VA. The autonomic nervous system and hypertension. SPb.: Meditsinskoe izdatel'stvo; 2008. Russian. Шляхто Е. В., Конради А. О., Цырлин В. А. Вегетативная нервная система и артериальная гипертензия. СПб.: Медицинское издательство; 2008. ISBN 0000 — 0000.

Chapter:

Nichols WW, O'Rourke MF. Aging, high blood pressure and disease in humans. In: Arnold E, ed. McDonald's Blood Flow in Arteries: Theoretical, Experimental and Clinical Principles. 3rd ed. London/ Melbourne/Auckland: Lea and Febiger; 1990. p.398 — 420. ISBN 0000 — 0000.

Russian chapter:

Diagnostics and treatment of chronic heart failure. In. National clinical guidelines 4th ed. Moscow: Silicea-Polygraf; 2011. pp.203 — 93. Russian Диагностика и лечение хронической сердечной недостаточности. В кн: Национальные клинические рекомендации. 4-е издание. М.: Силицея-Полиграф; 2011.сс.203 — 96. ISBN 0000 — 0000.

Webpage:

Panteghini M. Recommendations on use of biochemical markers in acute coronary syndrome: IFCC proposals. eJIFCC 14. http://www.ifcc.org/ejifcc/vol14no2/1402062003014n.htm (28 May 2004)

All sources of literature are checked for correctness through the system of the Russian electronic library. Significant errors in citation or duplication of the source are the reason for the return of the manuscript to the authors for revision.

VI. Preparation of manuscript.

The author prepares the following documents to upload the manuscript to the site:

The main file Is the text of the article (the system renames it after loading, so it does not matter how it is called).

Additional files-Directional (accompanying) letter, Information file with the Title page, information about the authors and disclosure of conflicts of interest, files with pictures.

For more information on placing articles on the website you can read http://cardiovascular.elpub.ru/jour/announcement

VII. Copyright and publishing policy.

This section regulates the relationship between the editorial Office (Publisher) of *International heart and vascular disease journal* (the "editorial Office") and the author or group of authors who submitted their manuscript for publication in the *International heart and vascular disease journal* (the "Author").

The author, by sending the article to the Editor, agrees that the editorial Board of the journal shall be transferred to the exclusive property rights to use the manuscript (transferred to the Editorial Board of the journal material, including such protected objects of copyright as photos of the author, drawings, diagrams, tables, etc.), including the reproduction in print and on the Internet; distribution; translation into any languages of the peoples of the world; export and import of copies of the journal with the article of the Author for distribution, to bring to the public.

The editorial Board reserves the right to reduce and edit the materials of the manuscript, to carry out scientific editing, to reduce and correct articles, to change the design of graphs, drawings and tables to bring into line with the design of the journal, without changing the meaning of the information provided.

When using the article, the editors have the right to supply it with any illustrated material, advertising and allow third parties to do so.

The editorial Board has the right to assign the rights received from the Author to third parties and has the right to prohibit third parties from any use of materials published in the journal for commercial purposes.

The author guarantees that he has exclusive rights to use the submitted material. In case of violation of this guarantee and the presentation of claims to the editorial Board, the Author independently and at his own expense undertakes to settle all claims. The editorial Board is not responsible to third parties for violation of the Author's guarantees.

The Author retains the right to use the published material, its fragments and parts for personal, including scientific and teaching purposes.

The Author transfers the above rights to the Editors without limitation of their validity period, in the territory of all countries of the world without limitation, including the territory of the Russian Federation.

The rights to the manuscript are considered to be transferred By the author of the editorial Office from the moment of sending an information letter about the acceptance of the manuscript to the press.

Reprinting of materials published in the journal by other individuals and legal entities is possible only with the written permission of the editorial Board, with the obligatory indication of the journal name, number and year of publication.

The editors are not responsible for the accuracy of the information provided by the Author.

The author, sending the manuscript to the Editor, gives permission to use and process personal data.

The editorial Board reserves the right to reduce and correct the articles, to change the design of graphs, figures and tables to comply with the standard of the journal, without changing the meaning of the information provided. In case of untimely response of the author (s) to the request of the editorial Board, the editorial Board may at its discretion make changes to the article or refuse to publish.

Sending to the editor of works that have already been sent to other publications or printed in them is absolutely not allowed. The editors are not responsible for the accuracy of the information provided by the authors. Articles sent in violation of the rules of registration are not accepted by the editorial Board for consideration.

VIII. The procedure for rewiewing manuscripts

The manuscript should be sent in electronic form to the Editor through the website — http://www.heart-vdj.com. The manuscript should be drawn up in accordance with these requirements for scientific articles submitted for publication in the journal.

The author is sent a notification letter of receipt of the manuscript with the number (ID), which will be used in subsequent correspondence. The author can track the stages of work on his manuscript through the site. Since the process of bringing the manuscript to the necessary standards takes enough expert time, the payment for the initial review of the article was introduced, which the author (s) are required to carry out after the article is posted on the site.

The manuscript must pass the primary selection: the Editorial Board has the right to refuse publication or send comments to the article, which must be corrected by the Author before reviewing.

— checking the completeness of the manuscript: if you do not comply with the requirements of the Rules for the authors to complete the manuscript or its design, the Editors have the right to refuse to publish or in writing to require to send the missing materials or to correct the version already downloaded to the site.

— Manuscripts are checked in the "Antiplagiat" system. The originality of the manuscript should be at least 75 %. We expect manuscripts submitted for publication to be written in an original style that involves new thinking without the use of previously published text. Manuscript with originality below 75 % shall not be admissible.

All manuscripts submitted to the journal are sent to one of the permanent reviewers or an independent expert according to the profile of the research.

The review process is anonymous both for the Author and for the reviewers. The manuscript is sent to the reviewer without the names of the authors and the name of the institution.

The editorial Board informs the Author of the results of the review by e-mail.

If the reviewer makes a conclusion about the possibility of publication of the article and does not make significant corrections, the article is given to the expert on statistics and after a positive report is accepted for further work.

If the reviewer makes a conclusion about the possibility of publication of the article and gives instructions on the need for its correction, the Editorial Board sends the review to the Author with a proposal to take into account the recommendations of the reviewer in the preparation of a new version of the ar-

ticle or to refute them. In this case, the Author needs to make changes to the last version of the article file, which is located on the site (download file from the site, make changes and place the corrected article again, after removing the primary (uncorrected) version). The revised article is re-sent for review, and the conclusion is given that all the recommendations of the reviewer were taken into account. After receiving a positive response of the reviewer, the article is given to the expert on statistics and after a positive report is accepted for further work.

If the reviewer makes a conclusion about the impossibility of publication of the article. The author of the reviewed work is given the opportunity to read the text of the review, if he does not agree with the conclusions of the reviewer. In case of disagreement with the opinion of the reviewer, the Author has the right to provide a reasoned response to the Editor. The article can be sent for re-review or for approval to the editorial Board. The editorial Board or its authorized editor shall send its response to the Author.

All manuscripts that have been reviewed and evaluated by an expert in statistics are submitted to the editorial Board, which decides on the publication. After the decision on the admission of article for publication, the Editorial office inserts the publication of the article in terms of publications. Information about the annual (thematic) plan of publications is placed on the website of the journal.

The decision to publish a manuscript is made solely on the basis of its significance, originality, clarity of presentation and compliance of the research topic with the direction of the journal. Reports on studies in which negative results are obtained or the provisions of previously published articles are challenged are considered on General grounds.

Original reviews are kept in the Editorial office for 5 years from the date of publication.

In case of a decision to refuse to publish an article, its archive copy remains in the electronic system of the editorial Board, but access to it by editors or reviewers is closed.

IX. The manner of publication of manuscripts

According to the requirements of the Higher attestation Commission, the journal provides priority for post-graduate and doctoral works, the period of their publication depends on the expected date of protection, which the authors must specify in the primary documents attached to the manuscript.

Each issue of the journal is formed by a separate Executive editor appointed by the editor-in-Chief and/or editorial Board. It is the responsibility of the editor-in-charge to select high-quality articles for publication, and he can be guided by both thematic principles and a separate scientific direction.

All selected articles are submitted to the scientific editor and proofreader. After creating the layout of the article and editing it, the article will be available to the Author through the site. At this stage, it will be possible to send comments on the text of the article. The author is obliged to send his / her consent to the publication or his / her comments within the established time specified in the cover letter.

The editorial office does not send the author's copy by mail or PDF of the article by e-mail, access to the published numbers is open.

Subscription to the printed version is carried out by half a year (through subscription agencies).

X. After the publication in the journal

Information on publication is distributed in the following scientific citation databases: Russian science citation index, CYBERLENINKA and others. The article is assigned a DOI index and the full text is publicly available on the journal's website.

Information about the publication of the issue is distributed by mailing of The Cardioprogress Foundation and in social networks.

We expect the authors of the articles to actively make efforts to bring the results of their research to the public, namely: to have a personal page on the Internet (personal page), to monitor and update your profile ORCID and RecsearcherID, to involve colleagues in their work through social networks.

XI. Revocation or correction of articles

The full text of the journal's policy on Revocation and correction of articles is available in the information section on the website. The editors follow COPE Recommendations issued by the Committee on publishing ethics (COPE) — http://www.publicationethics.org.uk. in cases:

Editors of journals should consider the opinion of the publication, if:

they have clear evidence of the unreliability of the information published, either as a result of conscious actions (for example, falsification of data), or due to good faith errors (for example, errors in calculations or experiments); the findings have been previously published in another publication and there is no proper reference, authorization and justification for re-publication (i.e. duplicate publication).); it is plagiarism;

describes unethical research.

Editors of journals should consider the concerns, if:

they received information about the authors ' inappropriate actions, but there is no clear evidence of such behavior; there are arguments that the results of the work are unreliable, and the institution in which the authors work is not going to find out the truth; they believe that the investigation into the alleged violations committed by the authors in connection with the publication has either not been or will not be fair, impartial and convincing; the authors ' violations are being investigated, but the results are not expected soon enough.

Journal editors should consider making amendments if:

a small part of the rest of the high-quality publication is unreliable (especially because of conscientious errors);

the list of authors / sponsors contains errors (i.e., it does not contain someone who is worthy to be an author, or a person who does not meet the authorship criteria).

In most cases, a review is not appropriate if:

authorship needs to be changed, but there is no reason to doubt the validity of the findings.

XII. Position E-log backup (if journal is no longer published)

The purpose of backup is to prevent loss of information in case of hardware, software, critical and crisis situations, etc.

Information of the following main categories is subject to backup: — personal information of authors (personal directories on file servers); — pdf of published articles; — information about literary links to the article in the DOI system.

All this information is publicly available in The system of the Russian citation index on the website of the Electronic library www.elibrary.ru

XIII. Journal subscription

Information on subscriptions is available on the journal website in the section "Subscription":

XIV. Journal subscription

The name of the journal in English is International heart and vascular disease journal.

Official sites where information about the journal is placed:

http://www.heart-vdj.com

On the reception of the articles, making decisions about publication, reviews — mmamedov@mail.ru

On organizational issues (working with the site, subscription) — editor.ihvdj@gmail.com

Editorial office:

Room 213, Building 2, Prospect Gostinichny 6, Moscow 127106, Russia

e-mail: editor.ihvdj@gmail.com

Submission Preparation Checklist

As part of the submission process, authors are required to check off their submission's compliance with all of the following items, and submissions may be returned to authors that do not adhere to these guidelines.

The manuscripts are accepted if has not been published or submitted for publication elsewhere.

The file of the submitted article is in the format of a Microsoft Word document. It does not contain the names of the authors and institutions.

Files with a letter of transmittal and General information have been prepared for upload to the site.

3.The cited literature is presented in full, framed by the Rules for the authors and does not contain duplicates. All references are indicated in the text of the article.

Text should be typed with an interval of one line spacing, font Times New Roman, 12 pt; to highlight the accents it is recommended to use italics rather than underlining (except Internet links). All images, graphics and tables are placed within the text according to the meaning of the particular part of text (and not at the end of the document).

Text should follow the stylistic and bibliography requirements as stated in Regulations located in the Part "About Us."

Please, remove the authors' names from the title of the article and other parts of the document to ensure the anonymity of reviewing.

Copyright Notice

Privacy Statement

Specified when registering the names and addresses will be used solely for technical purposes of a contact with the Author or reviewers (editors) when preparing the article for publication. Private data will not be shared with other individuals and organizations.

ISSN: 2309 — 0901 (Print)
ISSN: 2311 — 1631 (Online)

FOUNDATION FOR THE ADVANCEMENT OF CARDIOLOGY

"CARDIOPROGRESS"

knowledge, observation, action

Official website: www.cardioprogress.ru

Tel: 007 965 236 1600

Email: inf.cardio@gmail.com

Moscow, Russia