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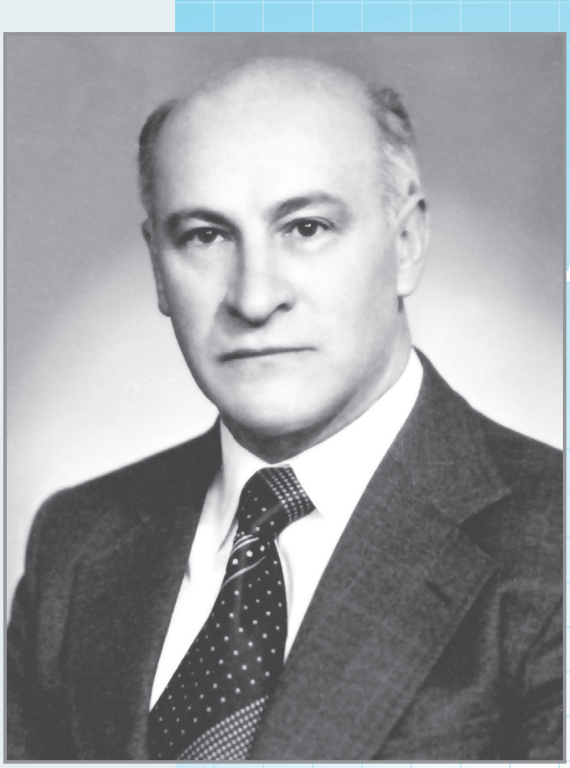

100 years since the birth of M.S. Kushakovsky

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МЕЖДУНАРОДНЫЙ МЕДИЦИНСКИЙ РЕЦЕНЗИРУЕМЫЙ ЖУРНАЛ

Издается под эгидой Евразийской аритмологической ассоциации врачей кардиологов и терапевтов

ЭКО • ВЕКТОР

CONTENTS

СОДЕРЖАНИЕ

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Dear colleagues!

The first issue of the journal that was initiated by the Eurasian Arrhythmology Association together with the Mechnikov North-Western State Medical University is now presented to the readers. The publications that focused on the problems of arrhythmias nowadays publish materials for a small target audience of doctors. This journal is intended for a wide range of specialists despite the impression of narrow specialization. This is a distinguishing characteristic of the journal. After all, heart rhythm and conduction disorders can often be manifestations of comorbid pathology.

The contemporary healthcare system cannot be developed without meaningful professional communication. We hope that the journal will become a debate platform for discussions on topical issues of heart diseases and comorbid conditions that are complicated by heart rhythm and conduction disorders. Moreover, we hope that it will help to ensure scientific communication and exchange of ideas and results of our research and contribute to the introduction of new scientific research results into healthcare practice. Currently, the conversational interaction and exchange of scientific knowledge enable arrhythmologists, cardiologists, cardiovascular surgeons, and scientists of other specialties to diversify clinical arrhythmology problems. We are convinced that such a multidisciplinary approach will significantly improve the quality of medical care for patients, not only with cardiac arrhythmias but also with various diseases that are the root cause or contribute to their development.

The journal publishes clinical guidelines, original articles, article reviews, clinical cases, lectures/discussion reports, and notes on the activities of the Eurasian Arrhythmology Association. All articles are subject to double-blind peer review by authoritative scientists and specialists reputable in the field of knowledge of the published article.

The journal is published in Russian and English quarterly, both in electronic and printed versions. All articles are translated by the publisher and are free for the authors of the publication.

On behalf of the editorial board, I proffer you close cooperation. We look forward to receiving articles and reviews from you.

Respectfully yours,
S.A. Saiganov

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Глубокоуважаемые коллеги!

Выпуск нашего журнала посвящен 100-летию со дня рождения профессора Макса Соломоновича Кушаковского (1922–2022), выдающегося кардиолога, ученого, Заслуженного деятеля науки РФ, Почетного доктора Санкт-Петербургской медицинской академии последипломного образования (в настоящее время — Северо-Западный государственный медицинский университет имени И.И. Мечникова).

Макс Соломонович автор многочисленных работ по кардиологии, большинство из которых не теряют своей актуальности и сегодня и имеют большое значение для современного сообщества кардиологов.

Профессор М.С. Кушаковский внес большой вклад в изучение вопросов этиологии, патогенеза, разработки современных методов диагностики и лечения нарушений сердечного ритма и проводимости, артериальной гипертензии и сердечной недостаточности.

Макс Соломонович Кушаковский создал мощную научную школу, которая до сих пор развивается в Северо-Западном государственном медицинском университете имени И.И. Мечникова.

С уважением,
главный редактор С. А. Сайганов

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Review

2022 Esc Guidelines for the Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death: What is New?

Tatiana N. Novikova, Vladimir I. Novikov, Sergey A. Saiganov, Vladislava A. Shcherbakova

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

The review presents new indications to help with diagnosis and treatment of ventricular arrhythmia (VA) in patients with various etiologies of rhythm disturbances, including patients with coronary artery disease, cardiomyopathies, channelopathies, inflammatory heart disease, neuromuscular disease, and congenital heart defects. Algorithms for diagnostic evaluation at first presentation with VAs in patients without known cardiac disease are given.

Keywords: ventricular arrhythmias; sudden cardiac death; algorithms for diagnostic evaluation at first presentation with ventricular arrhythmias.

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Обзорная статья

Европейские рекомендации по лечению пациентов с желудочковыми аритмиями и профилактике внезапной сердечной смерти 2022: что нового?

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

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

В обзоре представлена информация о новых показаниях, которыми следует руководствоваться при диагностике и лечении желудочковых нарушений ритма у пациентов с разной этиологией нарушений ритма, в том числе у пациентов, страдающих ишемической болезнью сердца, кардиомиопатиями, каналопатиями, воспалительными заболеваниями сердца, нейромышечными заболеваниями, врожденными пороками сердца, даны алгоритмы диагностической оценки при первом обращении пациента с желудочковыми нарушениями ритма без известных сердечных заболеваний.

Ключевые слова: желудочковые аритмии; внезапная сердечная смерть; алгоритмы диагностики при первом обращении пациента с желудочковыми нарушениями ритма.

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In the year of the 100th anniversary of the birth of the outstanding scientist, cardiologist, and arrhythmologist, Max Solomonovich Kushakovsky, new European guidelines for the treatment of patients with VAs and the prevention of sudden cardiac death (SCD) were published. Max Solomonovich Kushakovsky focused a lot of attention on the diagnosis and treatment of ventricular rhythm disturbances and lectured brilliantly on this problem.

Since the previous guidelines were released 7 years have passed, new approaches for diagnosing and treating VA have emerged. In this paper, only the key innovations will be highlighted.

The main new recommendations are presented in Table 1 [1].

Table 1. New key 2022 guidelines (Adapted from the 2022 European Society of Cardiology (ESC) Guidelines for the Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death [1])

Public basic life support and access to automated external defibrillators (AEDs)	Class
It is recommended that public-access defibrillation be available at sites where cardiac arrest (CA) is more likely to occur.[a]	I
Prompt cardiopulmonary resuscitation (CPR) by bystanders is recommended at out-of-hospital CA.	I
It is recommended to promote community training in basic life support to increase bystander CPR rate and AED use.	I
Mobile phone-based alerting of basic life support-trained bystander volunteers to assist nearby victims of out-of-hospital CA should be considered.	IIa
Ventricular arrhythmia (VA) treatment. General aspects	**Class**
Direct current cardioversion is recommended as the first-line treatment for patients presenting with tolerated sustained monomorphic ventricular tachycardia (SMVT) provided that the anesthetic/sedation risk is low.	I
Optimal medical treatment, including angiotensin-converting enzyme inhibitor/ angiotensin receptor blocker/ angiotensin receptor neprilysin inhibitor, mineralocorticoid receptor antagonist, and sodium–glucose co-transporter 2 inhibitors, is indicated in all heart failure patients with reduced ejection fraction (EF).	I
Implantation of a cardioverter defibrillator is only recommended in patients who have an expectation of good-quality survival >1 year.	I
In patients presenting with a hemodynamically tolerated SMVT and known or suspected structural heart disease (SHD), intravenous procainamide should be considered.	IIa
In patients presenting with a hemodynamically tolerated SMVT in the absence of an established diagnosis, intravenous amiodarone may be considered.	IIb
In patients with SMVT or sustained polymorphic ventricular tachycardia (SPVT)/ventricular fibrillation (VF) triggered by a premature ventricular complex (PVC) with similar morphology and an indication for implantable cardioverter defibrillator (ICD), catheter ablation may be considered when an ICD is not available, contraindicated for concurrent medical reasons, or declined by the patient.	IIb
The wearable cardioverter defibrillator may be considered in the early phase after myocardial infarction (MI) in selected patients.	IIb
Coronary artery disease (CAD)	**Class**
In patients with CAD and recurrent, symptomatic SMVT, or ICD shocks for SMVT despite chronic amiodarone therapy, catheter ablation is recommended in preference to escalating anti-arrhythmic drug (AAD) therapy.	I
Cardiac stress imaging during physical exercise is recommended in addition to cardiopulmonary exercise test after surgery in patients with anomalous aortic origin of a coronary artery with a history of aborted CA.	I
In sudden cardiac arrest (SCA) survivors with coronary artery spasm, implantation of an ICD should be considered.	IIa
ICD therapy should be considered in patients with CAD, New York Heart Association Class I, and left ventricular EF (LVEF) ⩽30% despite ⩾3 months of optimal medical treatment.	IIa
ICD implantation should be considered in patients with CAD, LVEF ⩽40% despite ⩾3 months of optimal medical treatment and non-sustained ventricular tachycardia (NSVT), if they are inducible for SMVT by programmed electrical stimulation (PES).	IIa
In patients with CAD and hemodynamically well-tolerated SMVT and LVEF ⩾40%, catheter ablation in experienced centers should be considered as an alternative to ICD therapy, provided that established endpoints have been reached.[b]	IIa
Catheter ablation should be considered in patients with CAD and recurrent, symptomatic SMVT, or ICD shocks for SMVT despite beta-blocker or sotalol treatment.	IIa

Continuation of the table 1

Idiopathic PVC/VT and PVC-induced cardiomyopathy	Class
Catheter ablation as first-line treatment is recommended for symptomatic idiopathic VT/PVCs from the right ventricle outflow tract (RVOT) or the left fascicles.	I
Beta-blockers or non-dihydropyridine calcium channel blockers are indicated in symptomatic patients with idiopathic VT/PVCs from an origin other than the RVOT or the left fascicles.	I
In patients with PVCs/VT with a presentation that is not typical for an idiopathic origin[c], cardiac magnetic resonance (CMR) should be considered, despite a normal echocardiogram.	IIa
Beta-blockers, non-dihydropyridine calcium channel blockers, or flecainide should be considered when catheter ablation is not available, not desired, or is particularly risky in symptomatic patients with idiopathic VT/PVCs from the RVOT or the left fascicles.	IIa
In symptomatic patients with idiopathic VT/PVCs from an origin other than the RVOT or the left fascicles, catheter ablation or flecainide should be considered.	IIa
In patients with an unexplained reduced EF and a PVC burden of at least 10%, PVC-induced cardiomyopathy should be considered.	IIa
CMR should be considered in patients with suspected PVC-induced cardiomyopathy.	IIa
In patients who do not respond to cardiac resynchronization therapy with frequent, predominately monomorphic PVCs limiting optimal biventricular pacing despite pharmacological therapy, catheter ablation or AADs should be considered.	IIa
Catheter ablation may be considered for idiopathic VT/PVCs in asymptomatic patients that repeatedly have more than 20% of PVCs per day at follow-up.	IIb
Amiodarone as a first-line treatment is not recommended in patients with idiopathic VTs/PVCs.	III

Dilated cardiomyopathy (DCM)/hypokinetic non-dilated cardiomyopathy (HNDCM)	Class
Genetic testing (including at least *LMNA, PLN, RBM20*, and *FLNC* genes) is recommended in patients with DCM/HNDCM and atrioventricular (AV) conduction delay at <50 years or who have a family history of DCM/HNDCM or SCD in a first-degree relative (at age <50 years).	I
In a first-degree relative of a DCM/HNDCM patient, an electrocardiogram (ECG), and an echocardiogram are recommended if: the index patient was diagnosed <50 years of age or has clinical features suggestive of an inherited cause, or there is a family history of DCM/HNDCM or premature unexpected sudden death (SD).	I
CMR with late gadolinium enhancement (LGE) should be considered in DCM/HNDCM patients for assessing the etiology and the risk of VA/SCD.	IIa
Genetic testing (including at least *LMNA*, *PLN*, *RBM20*, and *FLNC* genes) should be considered for risk stratification in patients with apparently sporadic DCM/HNDCM, who present at young age or with signs suspicious for an inherited etiology.	IIa
ICD implantation should be considered in DCM/HNDCM patients with an LVEF <50% and ≥2 risk factors (syncope, LGE on CMR, inducible SMVT at PES, and pathogenic mutations in *LMNA*, *PLN*, *FLNC*, and *RBM20* genes).	IIa
ICD implantation should be considered in patients with DCM/HNDCM and hemodynamically tolerated SMVT.	IIa
In a first-degree relative of a patient with apparently sporadic DCM/HNDCM, an ECG and an echocardiogram may be considered.	IIb
Participation in high-intensity exercise including competitive sports is not recommended for individuals with DCM/HNDCM and an *LMNA* mutation.	III

Arrhythmogenic right ventricular cardiomyopathy (ARVC)	Class
CMR is recommended in patients with suspected ARVC.	I
In patients with a suspected or definite diagnosis of ARVC, genetic counseling and testing are recommended.	I
ICD implantation should be considered in symptomatic[d] patients with definite ARVC, moderate right or left ventricular (LV) dysfunction, and either NSVT or inducibility of SMVT at PES.	IIa
In ARVC patients with indication for ICDs, a device with the capability of anti-tachycardia pacing programming for SMVT up to high rates should be considered.	IIa
Avoidance of high-intensity[e] exercise may be considered in carriers of ARVC-related pathogenic mutations and no phenotype.	IIb
Beta-blocker therapy may be considered in all patients with a definite diagnosis of ARVC.	IIb
In patients with ARVC and symptoms highly suspicious for VA, PES may be considered for risk stratification.	IIb

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Continuation of the table 1

Hypertrophic cardiomyopathy (HCM)	Class
CMR with LGE is recommended in HCM patients for diagnostic work-up.	I
Genetic counseling and testing are recommended in HCM patients.	I
In a first-degree relative of a patient with HCM, ECG and an echocardiogram are recommended.	I
ICD implantation should be considered in HCM patients aged 16 years or more with an intermediate 5-year risk of SCD (⩾ 4% to < 6%)[f], and with (a) significant LGE at CMR (usually ⩾15% of LV mass); or (b) LVEF <50%; or (c) abnormal blood pressure response during exercise test[g]; or (d) LV apical aneurysm; or (e) presence of sarcomeric pathogenic mutation.	IIa
ICD implantation should be considered in children <16 years of age with HCM with an estimated 5-year risk of SD ⩾ 6% (based on HCM Risk-Kids score[h]).	IIa
ICD implantation should be considered in patients with HCM presenting with hemodynamically tolerated SMVT.	IIa
In patients with HCM and recurrent, symptomatic VA, or recurrent symptomatic ICD therapy, AAD treatment should be considered.	IIa
Participation in high-intensity exercise may be considered for asymptomatic adult HCM patients without risk markers.	IIb
ICD implantation may be considered in HCM patients aged 16 years or more with a low estimated 5-year risk of SCD (<4%),[f] and with (a) significant LGE at CMR (usually ⩾15% of LV mass); or (b) LVEF <50%; or (c) LV apical aneurysm.	IIb
Catheter ablation in specialized centers may be considered in selected patients with HCM and recurrent, symptomatic SMVT, or ICD shocks for SMVT, in whom AADs are ineffective, contraindicated, or not tolerated.	IIb

LV non-compaction (LVNC) and restrictive cardiomyopathy	Class
In patients with an LVNC cardiomyopathy phenotype based on CMR or echocardiography, implantation of an ICD for primary prevention of SCD should be considered to follow DCM/HNDCM recommendations.	IIa
An ICD should be considered in patients with light-chain amyloidosis or transthyretin-associated cardiac amyloidosis and hemodynamically not tolerated VT.	IIa

Neuromuscular diseases	Class
Invasive electrophysiological evaluation (IEE) is recommended in patients with myotonic dystrophy and palpitations or syncope suggestive of VA or surviving a CA.	I
ICD implantation is recommended in patients with myotonic dystrophy and SMVT or aborted CA not caused by bundle branch re-entrant ventricular tachycardia (BBR-VT).	I
IEE should be considered in patients with myotonic dystrophy and a sudden increase in the PR interval or QRS duration.	IIa
IEE should be considered in patients with myotonic dystrophy and a PR interval ⩾240 ms or QRS duration ⩾120 ms, who are older than 40 years and have supraventricular arrhythmias, or who are older than 40 years and have significant LGE on CMR.	IIa
In myotonic dystrophy patients without AV conduction delay and a syncope that is highly suspicious for VA, ICD implantation should be considered.	IIa
In myotonic dystrophy patients with palpitations that are highly suspicious for VA and induction of a non-BBR-VT, ICD implantation should be considered.	IIa
In patients with limb-girdle type 1B or Emery–Dreifuss muscular dystrophies and indication for pacing, ICD implantation should be considered.	IIa
Implantation of an ICD may be considered in patients with Duchenne/Becker muscular dystrophy and significant LGE at CMR.	IIb
Implantation of an ICD over a permanent pacemaker may be considered in myotonic dystrophy patients with additional risk factors[i] for VA and SCD.	IIb
In patients with myotonic dystrophy, serial electrophysiological evaluation of AV conduction and arrhythmia induction is not recommended without arrhythmia suspicion or progression of ECG conduction disorders.	III

Continuation of the table 1

Inflammatory diseases	Class
In patients with hemodynamically NSVT or VF during the acute phase of myocarditis, ICD implantation before hospital discharge should be considered.	IIa
In post-myocarditis patients with recurrent, symptomatic VT, AAD treatment should be considered.	IIa
Catheter ablation performed in specialized centers should be considered in post-myocarditis patients with recurrent, symptomatic SMVT, or ICD shocks for SMVT in whom AADs are ineffective, not tolerated, or not desired.	IIa
ICD implantation should be considered in patients with hemodynamically tolerated SMVT occurring in the chronic phase of myocarditis.	IIa
In patients with cardiac sarcoidosis who have an LVEF >35%, but significant LGE at CMR after resolution of acute inflammation, ICD implantation should be considered.	IIa
In patients with cardiac sarcoidosis, who have an LVEF 35%–50% and minor LGE at CMR, after resolution of acute inflammation, PES for risk stratification should be considered.	IIa
In patients with cardiac sarcoidosis, LVEF 35%–50%, and inducible SMVT at PES, ICD implantation should be considered.	IIa
In patients with cardiac sarcoidosis and recurrent, symptomatic VA, AAD treatment should be considered.	IIa
Amiodarone should be considered to reduce arrhythmia burden in patients with Chagas' cardiomyopathy who present with symptomatic PVCs or VT.	IIa
In patients with Chagas' cardiomyopathy and recurrent, symptomatic SMVT, or ICD shocks for SMVT in whom AADs are ineffective, contraindicated, or not tolerated, catheter ablation in specialized centers should be considered.	IIa
In patients with hemodynamically well-tolerated SMVT occurring in the chronic phase of myocarditis, preserved LV function and a limited scar amenable to ablation, catheter ablation may be considered as an alternative to ICD therapy, after discussion with the patient and provided that established endpoints have been reached.[b]	IIb
Catheter ablation in specialized centers may be considered in cardiac sarcoidosis ICD recipients with recurrent, symptomatic SMVT, or ICD shocks for SMVT, in whom AADs are ineffective, contraindicated, or not tolerated.	IIb

Congenital heart disease (CHD)	Class
Evaluation for residual lesions or new structural abnormalities is recommended in patients with CHD presenting with sustained VAs.	I
In selected patients with CHD (including atrial baffle repair for transposition of the great arteries, Fontan operation, and Ebstein anomaly) presenting with CA, evaluation and treatment of supraventricular tachycardia with rapid ventricular conduction should be considered.	IIa
In patients with repaired tetralogy of Fallot (TOF) undergoing surgical or transcutaneous pulmonary valve replacement, pre-operative catheter mapping, and transection of VT-related anatomical isthmuses before or during the intervention may be considered.	IIb
In patients with repaired TOF, a preserved biventricular function, and symptomatic SMVT, catheter ablation or concomitant surgical ablation performed in specialized centers may be considered as an alternative to ICD therapy.	IIb

Idiopathic VF	Class
It is recommended that idiopathic VF is diagnosed in a SCA survivor, preferably with documentation of VF, after exclusion of an underlying structural, channelopathic, metabolic, or toxicological etiology.	I
Isoproterenol infusion, verapamil, or quinidine for acute treatment of an electrical storm or recurrent ICD discharges should be considered in idiopathic VF.	IIa
Quinidine should be considered for chronic therapy to suppress an electrical storm or recurrent ICD discharges in idiopathic VF.	IIa
Clinical testing (history, ECG, and high precordial lead ECG, exercise test, and echocardiogram) of first-degree family members of idiopathic VF patients may be considered.	IIb
In idiopathic VF patients, genetic testing of genes related to channelopathy and cardiomyopathy may be considered.	IIb

Long QT syndrome (LQTS)	Class
In patients with clinically diagnosed LQTS, genetic testing and genetic counseling are recommended.	I
Beta-blockers, ideally non-selective beta-blockers (nadolol or propranolol), are recommended in LQTS patients with documented QT interval prolongation to reduce risk of arrhythmic events.	I
Mexiletine is indicated in LQT3 patients with a prolonged QT interval.	I
In LQTS, it should be considered to calculate the arrhythmic risk before initiation of therapy based on the genotype and the duration of QTc interval.	IIa
ICD implantation may be considered in asymptomatic LQTS patients with high-risk profile (according to the 1-2-3-LQTS-Risk calculator) in addition to genotype-specific medical therapies (mexiletine in LQT3 patients).	IIb
Routine diagnostic testing with epinephrine challenge is not recommended in LQTS.	III

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Continuation of the table 1

Andersen–Tawil syndrome (ATS)	Class
Genetic testing is recommended in patients with suspected ATS.	I
ICD implantation is recommended in ATS patients after aborted CA or not tolerated sustained VT.	I
ATS should be considered in patients without SHD who present with at least two of the following: - Prominent U waves with or without prolongation of the QT interval. - Bidirectional and/or polymorphic PVCs/VT. - Dysmorphic features. - Periodic paralysis. - KCNJ2 pathogenic loss of function mutation.	IIa
Beta-blockers and/or flecainide with or without acetazolamide should be considered in ATS patients to treat VA.	IIa
An implantable loop recorder (ILR) should be considered in ATS patients and unexplained syncope.	IIa
ICD implantation may be considered in ATS patients who have a history of unexplained syncope or suffer from tolerated sustained VT.	IIb

Brugada syndrome (BrS)	Class
Genetic testing for *SCN5A* gene is recommended for probands with BrS.	I
BrS should be considered in patients with no other heart disease and induced type 1 Brugada pattern who have at least one of the following: - Arrhythmic syncope or nocturnal agonal respiration. - A family history of BrS. - A family history of SD (< 45 years) with a negative autopsy and circumstance suspicious for BrS.	IIa
Implantation of a loop recorder should be considered in BrS patients with an unexplained syncope.	IIa
BrS may be considered as a diagnosis in patients with no other heart disease who exhibit an induced type 1 Brugada ECG.	IIb
PES may be considered in asymptomatic patients with a spontaneous type I BrS ECG.	IIb
Sodium channel blocker test is not recommended in patients with a prior type I Brugada pattern.	III
Catheter ablation in asymptomatic BrS patients is not recommended.	III

Early repolarization syndrome (ERS)	Class
It is recommended that the early repolarization pattern (ERP) is diagnosed as J-point elevation of ⩾ 1 mm in two adjacent inferior and/or lateral ECG leads.	I
It is recommended that the ERS is diagnosed in a patient resuscitated from unexplained VF/polymorphic VT (PVT) in the presence of ERP.	I
ICD implantation is recommended in patients with a diagnosis of ERS who have survived a CA.	I
In a SCD victim with a negative autopsy and medical chart review, and an ante-mortem ECG demonstrating the ERP, the diagnosis of ERS should be considered.	IIa
First-degree relatives of ERS patients should be considered for clinical evaluation for ERP with additional high-risk features.[j]	IIa
ILR should be considered in individuals with ERP and at least one risk feature[k] or arrhythmic syncope.	IIa
Isoproterenol infusion should be considered for ERS patients with electrical storm.	IIa
Quinidine in addition to an ICD should be considered for recurrent VF in ERS patients.	IIa
PVC ablation should be considered in ERS patients with recurrent VF episodes triggered by similar PVC non-responsive to medical treatment.	IIa
Genetic testing in ERS patients may be considered.	IIb
ICD implantation or quinidine may be considered in individuals with ERP and arrhythmic syncope and additional risk features.[k]	IIb
ICD implantation or quinidine may be considered in asymptomatic individuals who demonstrate a high-risk ERP[j] in the presence of a family history of unexplained juvenile SD.	IIb
Clinical evaluation is not recommended routinely in asymptomatic subjects with ERP.	III
ICD implantation is not recommended in asymptomatic patients with an isolated ERP.	III

End of Table 1

Catecholaminergic polymorphic VT (CPVT)	Class
Genetic testing and genetic counseling are indicated in patients with clinical suspicion or clinical diagnosis of CPVT.	I
Beta-blockers, ideally non-selective (nadolol or propranolol), are recommended in all patients with a clinical diagnosis of CPVT.	I
Epinephrine or isoproterenol challenge may be considered for the diagnosis of CPVT when an exercise test is not possible.	IIb

Short QT syndrome (SQTS)	Class
Genetic testing is indicated in patients diagnosed with SQTS.	I
SQTS should be considered in the presence of a QTc ⩽ 320 ms.	IIa
SQTS should be considered in the presence of a QTc ⩾ 320 and ⩽ 360 ms and arrhythmic syncope.	IIa
ILR should be considered in young SQTS patients.	IIa
ICD implantation should be considered in SQTS patients with arrhythmic syncope.	IIa
SQTS may be considered in the presence of a QTc ⩾320 and ⩽360 ms and a family history of SD at age < 40 years.	IIb
Quinidine may be considered in (a) SQTS patients who qualify for an ICD, but present a contraindication to the ICD or refuse it, and (b) asymptomatic SQTS patients and a family history of SCD.	IIb
Isoproterenol may be considered in SQTS patients with an electrical storm.	IIb

Selected populations	Class
It is recommended that athletes diagnosed with a cardiovascular disease associated with SCD are managed according to current guidelines for sports eligibility.	I
Continuation of beta-blockers should be considered during pregnancy in women with ARVC.	IIa
Oral metoprolol, propranolol, or verapamil should be considered for long-term management of idiopathic sustained VT during pregnancy.	IIa
Catheter ablation using non-fluoroscopic mapping systems should be considered, preferably after the first trimester, in women with highly symptomatic recurrent SMVT refractory or who are intolerant to AADs.	IIa

New sections appeared in the 2022 guidelines [1]:

1. Provocative diagnostic tests.
2. Genetic testing.
3. Diagnostic evaluation at first presentation with VA in patients without known cardiac disease.
4. Management of electrical storm and incessant VT.
5. Special aspects of device therapy.

Provocative diagnostic tests, in particular, include the following recommendations:

- Sodium channel blocker testing for BrS.
- Adenosine test to exclude latent pre-excitation.
- Epinephrine challenge may be useful in CPVT when exercise cannot be performed.
- Coronary vasospasm as a cause of VF in the absence of obstructive coronary diseases/cardiomyopathy can be tested with incremental intracoronary doses of acetylcholine/ergonovine.

The usefulness of stress and genetic testing is emphasized in LQTS. In contrast, epinephrine test is not recommended due to the high false positive rate and utility of exercise testing.

In the section “Genetic testing,” a table “Genetic tests and suggested work-up of probands and relatives with primary electrical diseases” is given. For suspected disorders, such as LQTS, BrS, and CPVT, genetic testing (Class I), including neonatal genetic testing for LQTS and CPVT, is recommended [1].

Detailed diagnostic flowcharts are given in the section “Diagnostic evaluation at first presentation with ventricular arrhythmia in patients without known cardiac disease”, and five frequently encountered clinical scenarios of diagnostic search are highlighted. This section is crucial because first-time ventricular rhythm disturbances can be a predictor of an unfavorable prognosis. The nature of the arrhythmia and its cause must be identified as soon as possible to avoid premature patient death in recurrent malignant VAs. The algorithms listed in the recommendations provide a rapid and targeted diagnostic search. The last two scenarios focus on the identification of the causes of death in patients who died due to SCD and examination and management of their relatives. Emphasis is placed on the search for genetic diseases and the prevention of SCD in relatives.

Scenario 1: Incidental finding of NSVT

An algorithm for the evaluation of patients presenting with an incidental finding of NSVT is presented in Figure 1.

Incidental NSVT is frequently discovered during routine cardiological evaluation (e.g., for non-cardiac diseases, pre-initiation of oncological treatments, and pre-participation in sports) and monitoring before induction of anesthesia/sedation for non-cardiac procedures [2]. Patients with incidentally found NSVT require further evaluation. Recent syncope suspicious for cardiac origin is a high-risk symptom

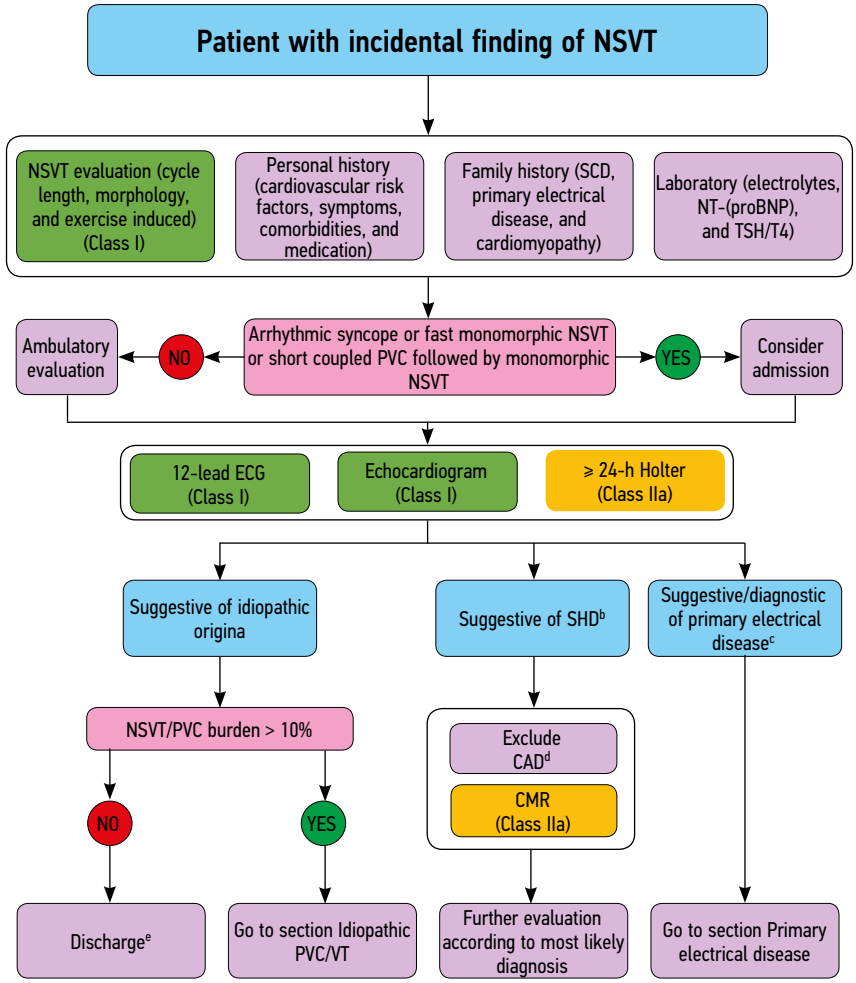

Fig. 1. Algorithm for the evaluation of patients presenting with an incidental finding of non-sustained ventricular tachycardia (adapted from the 2022 ESC Guidelines for the Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death) [1]. CAD, coronary artery disease; CMR, cardiac magnetic resonance; ECG, electrocardiogram; NSVT, non-sustained ventricular tachycardia; PVC, premature ventricular complex; SCD, sudden cardiac death; SHD, structural heart disease; NT-(proBNP), N-terminal pro-brain natriuretic peptide; VT, ventricular tachycardia; TSH/T4, thyroid hormone/thyroxine.
[a] ECG morphology suggestive of RVOT or fascicular origin, negative family history, normal 12-lead ECG, and an echocardiogram. [b] Atrioventricular conduction abnormalities, Q waves, broad QRS complex, ST/T waves deviations, and abnormally high or low voltages. Ventricular dysfunction/dilatation/hypertrophy/wall thinning, wall motion abnormalities, multitopic PVCs/NSVTs/increasing VA burden with exercise. [c] Brugada pattern, long/short QT, polymorphic/bidirectional VA with exercise. [d] Diagnostic test to exclude CAD according to patient profile and symptoms. [e] Consider re-evaluation in case of new symptoms or changes in patient clinical condition.

and may prompt admission to hospital [3, 4]. The morphology of NSVT (polymorphic or monomorphic) is important to assess. Typical morphology of benign monomorphic VT can suggest an idiopathic origin with favorable prognosis (Fig. 2, 3) [1]. In contrast, short coupled PVC initiating non-sustained PVT or monomorphic NSVT with short cycle length (usually < 300 ms, average 245 ± 28, in one series) may identify patients at higher risk of SCD [5, 6].

The following diagnostic search for the causes of NSVT is proposed:

- Resting 12-lead ECG is a first-line evaluation and may show signs of SHD, for example, LV myocardial hypertrophy or primary electrical diseases [7].
- Echocardiography is the first-line imaging modality that provides important information about cardiac function and potential SHD [8–10].
- Holter monitoring can be used to determine the frequency of NSVT and related PVCs [11]. In addition, an at least 3-lead Holter (V1, two inferior leads) may provide a first estimate if NSVT/PVC are unifocal or multifocal and of the NSVT site(s) of origin. The latter is important if the NSVT has not been previously documented on a 12-lead ECG [12].
- An exercise test can be helpful to capture the 12-lead ECG of NSVT and to identify exercise induced arrhythmias. Increased arrhythmias with exercise, not suggestive of idiopathic origin, should raise the possibility of SHD and may necessitate advice to refrain from physical exercise until diagnosis and initiation of appropriate treatment. Underlying significant CAD should be ruled out according to the patient's pre-test probability.

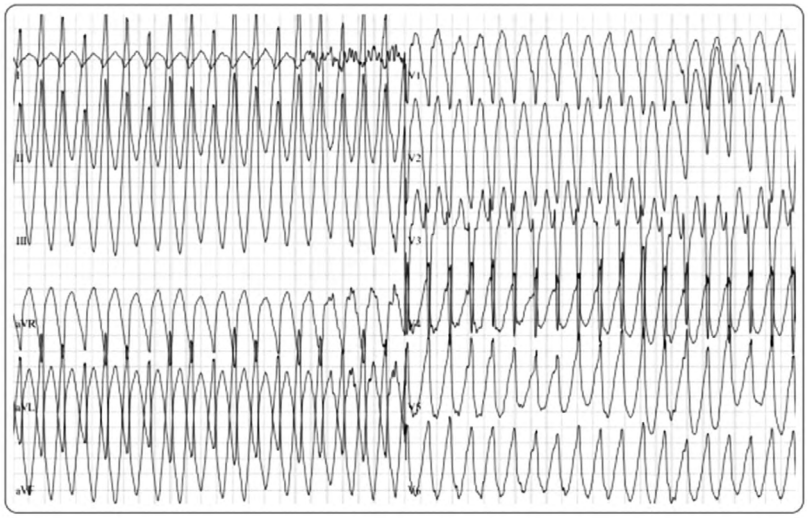

Fig. 2. Ventricular tachycardia of the right ventricle outflow tract (left bundle branch block-like QRS morphology, inferior axis, V4 transition) [1].

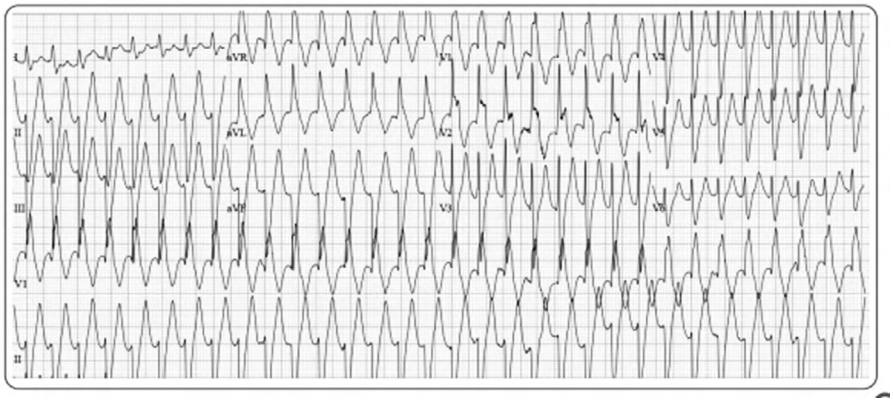

Fig. 3. Fascicular ventricular tachycardia (right bundle branch block-like QRS morphology, superior axis, QRS 130 ms) [1].

- CMR should be considered when cardiomyopathies or inflammatory diseases are suspected on initial evaluation. In addition, CMR can identify areas of fibrosis as substrates of NSVT [13, 14].

Scenario 2: Manifestation of SMVT

An algorithm for the evaluation of patients presenting with a first SMVT episode is presented in Figure 4.

The majority of patients presenting with SMVT have underlying SHD. SMVT in SHD is mainly due to scar-related re-entry and only occasionally due to re-entry involving a diseased conduction system or due to focal sources.

The diagnostic algorithm begins with the identification of the underlying pathology, and, in its absence, with confirmation of the diagnosis of idiopathic VT. Initial evaluation includes a comprehensive clinical and family history, 12-lead ECG, and echocardiography. Recording of the 12-lead VT ECG is indicated as it provides important information on the VT site of origin. Specific VT morphologies (e.g., RVOT or fascicular origin) in the absence of a family history for cardiomyopathies and without evidence for SHD are suggestive for idiopathic VTs [15]. Atypical ECG morphologies and uncommon clinical presentations should raise suspicions for underlying SHD even if baseline ECG and echocardiogram are normal. In this scenario, additional evaluation with CMR should be considered [16]. BBR-VT, resembling bundle branch block configuration on the ECG, is a feature of DCM, myotonic dystrophy, and post-cardiac valve surgery (Fig. 5).

A CAG can exclude significant CAD if initial evaluation raises suspicion of underlying CAD. If ECG and echocardiography are suggestive for a cardiomyopathy, CMR provides important diagnostic information on scar distribution and tissue characteristics. When non-invasive evaluation is inconclusive, electroanatomical mapping and PES may be considered for the differential diagnosis between idiopathic VT and early ARVC [17]. Electroanatomical mapping-guided biopsy can be of value to provide a tissue diagnosis for ARVC and inflammatory diseases with a focal distribution (e.g., cardiac sarcoidosis) [18, 19]. In cases of suspected inflammatory diseases, positron emission tomography CT, autoimmune serology, and biopsies of affected tissue are part of the diagnostic evaluation [20, 21].

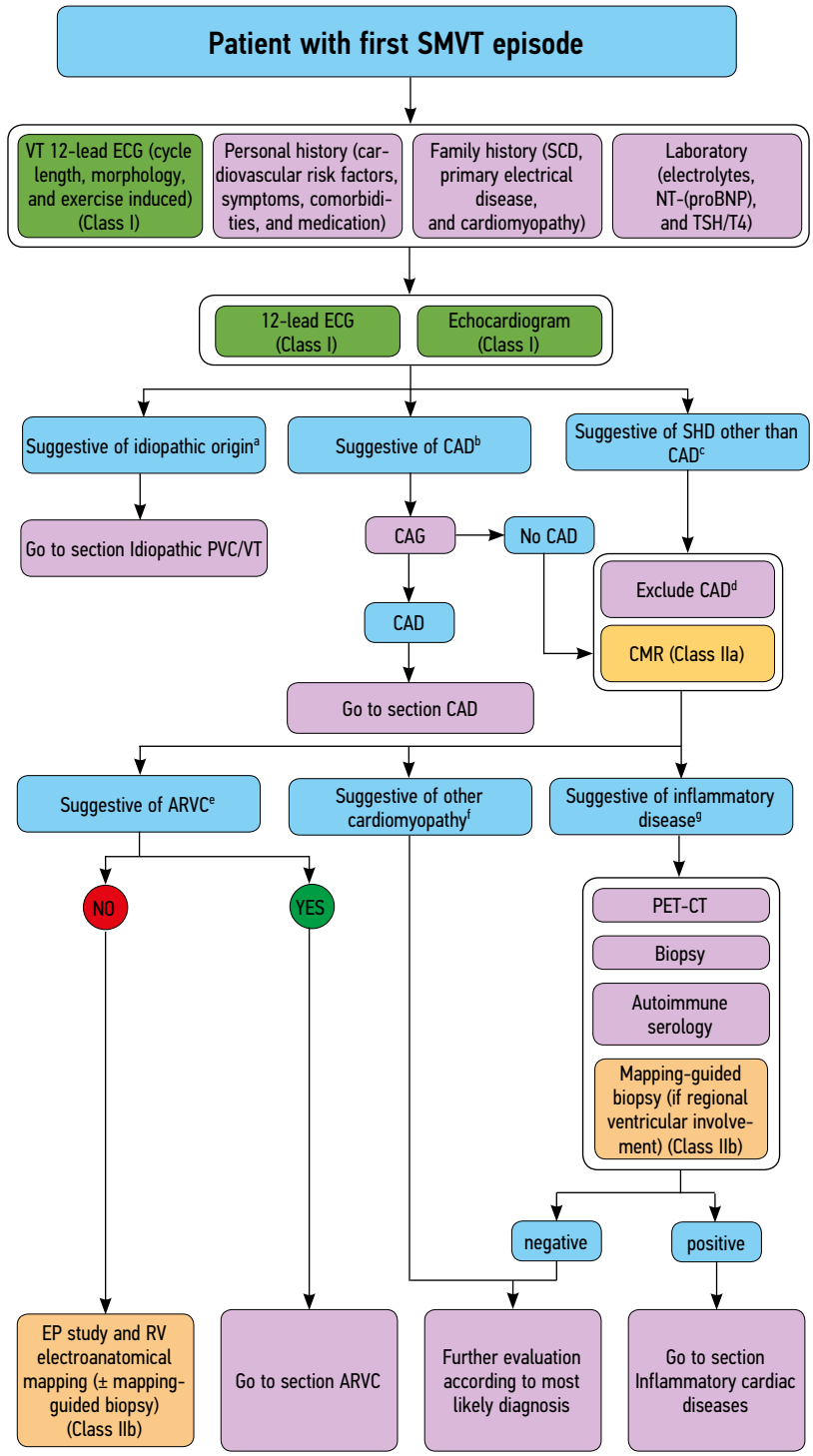

Fig. 4. Algorithm for the evaluation of patients presenting with a first sustained monomorphic ventricular tachycardia episode (adapted from the 2022 ESC Guidelines for the Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death) [1]. ARVC, arrhythmogenic RV cardiomyopathy; CAD, coronary artery disease; CAG, coronary angiography; CMR, cardiac magnetic resonance; ECG, electrocardiogram; EP, electrophysiological; LV, left ventricular; PET-CT, positron emission tomography and computed tomography; PVC, premature ventricular complex; RV, right ventricular; SCD, sudden cardiac death; SHD, structural heart disease; SMVT, sustained monomorphic ventricular tachycardia; VT, ventricular tachycardia. [a] ECG morphology suggestive of RV outflow tract or fascicular origin, negative family history, normal 12-lead ECG, and echocardiogram. [b] Q waves, QRS fragmentation, ST/T abnormalities, wall motion abnormalities in coronary territories. [c] AV conduction abnormalities, Q waves, broad QRS complex, T wave inversion, abnormally high or low voltages. Ventricular dysfunction/dilatation/hypertrophy/wall thinning/wall motion abnormalities/diffuse hypokinesia. [d] Diagnostic test to exclude CAD according to patient profile and symptoms. [e] According to revised task force criteria.
[f] AV conduction abnormalities, abnormally high or low voltages, broad QRS, ST/T wave deviations, LV dilatation and dysfunction, and late gadolinium enhancement with non-ischemic distribution. [g] AV conduction abnormalities, broad QRS, ST/T deviations, multifocal PVCs, inflammatory hyperemia and edema, fibrosis, left and right ventricular systolic dysfunction, and pericardial effusion.

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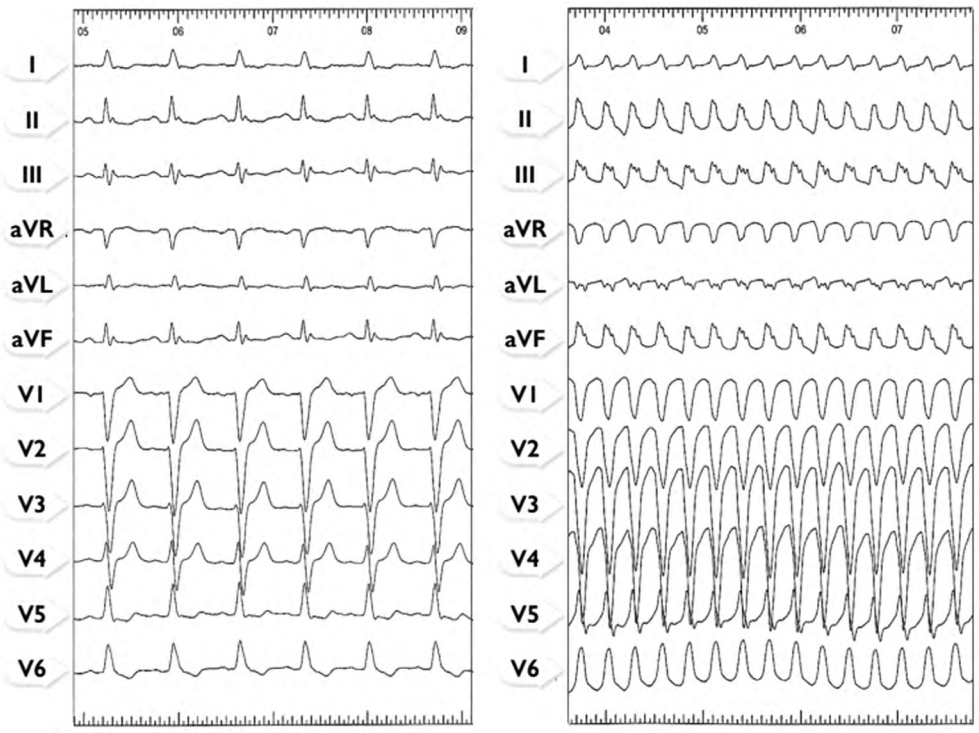

Fig. 5. Bundle branch re-entrant ventricular tachycardia. Left, ECG during sinus rhythm; right, ECG during tachycardia [1].

Scenario 3: SCA survivors

An algorithm for the evaluation of SCA survivors is presented in Figure 6.

Primarily, this situation can be observed in patients with an acute MI. Urgent CAG is recommended for patients presenting with ST-elevation MI [22–25]. Data on the appropriateness of urgent CAG for MI without ST-elevation are contradictory [26–30]. Three randomized controlled trials have found no significant benefit for early CAG in CA without ST-elevation. In case of electrical instability after CA, suspicious for ongoing ischemia, this panel found a CAG indicated.

Brain and chest CT scan may acutely identify non-cardiac causes of aborted SD (e.g., stroke, pulmonary embolism, and aortic dissection) [31].

Patients surviving SCA are advised to perform toxicological blood tests [32–34]. Retention and storage of suitable blood samples will allow subsequent diagnostic evaluation, including DNA analysis [32].

ECG plays an important role in the diagnosis. Any ECG tracing from emergency services, as well as recordings from interrogation of cardiovascular implantable electronic devices can also contribute to the diagnosis [35–38].

The resting 12-lead ECG, which includes high precordial lead, is fundamental and should be repeated regularly during recovery [39]. In addition, until definite treatment, continuous heart rhythm monitoring is recommended [40, 41].

Echocardiography may allow early diagnosis to identify any structural abnormality [41, 42].

Coronary imaging will be important to exclude CAD, dissection, or anomalies [43, 44]. Coronary optical coherence tomography and/or intravascular ultrasound may be helpful to characterize stenosis/plaque stability and underlying mechanism of stenosis [45].

It has been repeatedly shown that CMR provides significant incremental diagnostic value. Particularly, in the absence of changes typical for cardiomyopathies according to other methods of investigation (ECG and echocardiogram), CMR can reveal early stages of structural changes in cardiomyopathies, especially in ARVC [46, 47]. The role of CMR in detecting such structural abnormalities in mitral valve prolapse as papillary muscle fibrosis and mitral annular disjunction is emphasized [48, 49]. The shortcomings of the recommendations include the absence of validated criteria for stratifying the risk of sudden death in patients with mitral valve prolapse and mitral annular disjunction and absence of references to the 2020 Padua criteria for ARVC diagnosis.

Primary electrical diseases may be uncovered by provocative maneuvers, such as sodium channel blocker challenge, [50–53], adenosine challenge, [54, 55], epinephrine challenge [56–62], ergonovine/acetylcholine [63, 64], mental stress [65, 66], and exercise testing [67–71].

Electrophysiological study and electroanatomic mapping may be useful to provide patient-specific insights into the mechanism of CA and to offer therapeutic options in some patients [72–76].

Genetic testing may identify a molecular cause of SCA by revealing pathogenic mutations in genes associated with specific phenotypes. Primarily, genetic testing can help identify channelopathies [77, 78].

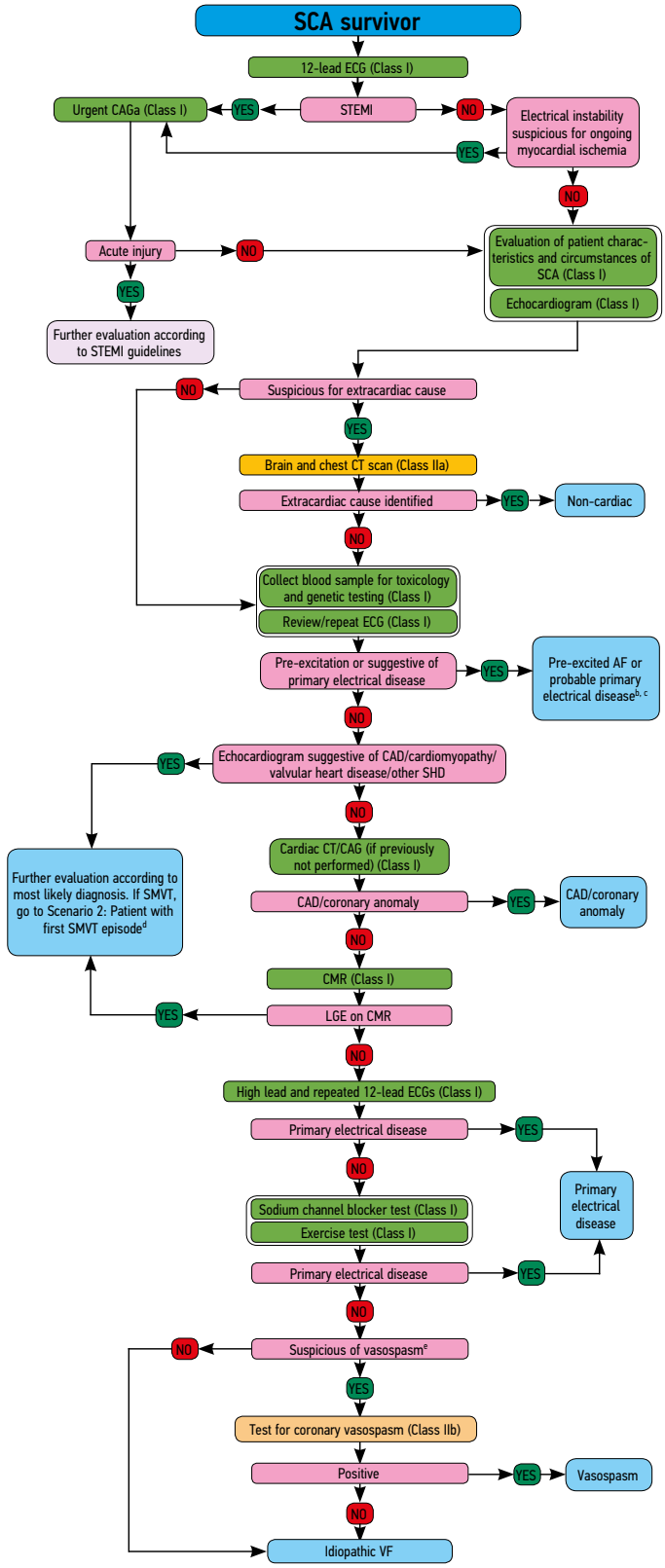

Fig. 6. Algorithm for the evaluation of sudden cardiac arrest survivors (adapted from the 2022 ESC Guidelines for the Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death) [1]. AF, atrial fibrillation; CAD, coronary artery disease; CAG, coronary angiogram; CMR, cardiac magnetic resonance; CT, computed tomography; ECG, electrocardiogram; LGE, late gadolinium enhancement; SCA, sudden cardiac arrest; SHD, structural heart disease; SMVT, sustained monomorphic ventricular tachycardia; STEMI, ST-elevation myocardial infarction; VF, ventricular fibrillation: [a] The 2017 ESC Guidelines for the Management of Acute Myocardial Infarction in Patients Presenting with ST-Segment Elevation. [b] Rule out SHD according to patient age and characteristics; QT duration needs to be reassessed several days after arrest. [c] Consider cardiac CT/CAG depending on patient characteristics and clinical context. [d] LV function on echocardiogram needs to be reassessed several days after arrest to exclude stunning as cause of systolic dysfunction. [e] In case of high clinical suspicion (typical symptoms and transient ST-elevation during monitoring), it can be considered to test for coronary vasospasm earlier.

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Scenario 4: SD victims

An algorithm for the evaluation of SD victims is presented in Figure 7.

Potential genetic cardiac disease can be identified in 25%–49% of SCD cases in the young (<50 years of age) [79–81]. This may also affect family members of the deceased. To determine the cause of death, it is important to collect all available data on prior symptoms, comorbidities, and family history. The main role of autopsy in SD is to establish the cause of death. Inherited cardiac diseases identified at autopsy include cardiomyopathies (HCM, DCM, and ARVC) and premature CAD [79–83]. A toxicology screen can reveal drug overdose or polypharmacy in 31%–56% of young SD cases. Another cause of SCD is primary electrical diseases

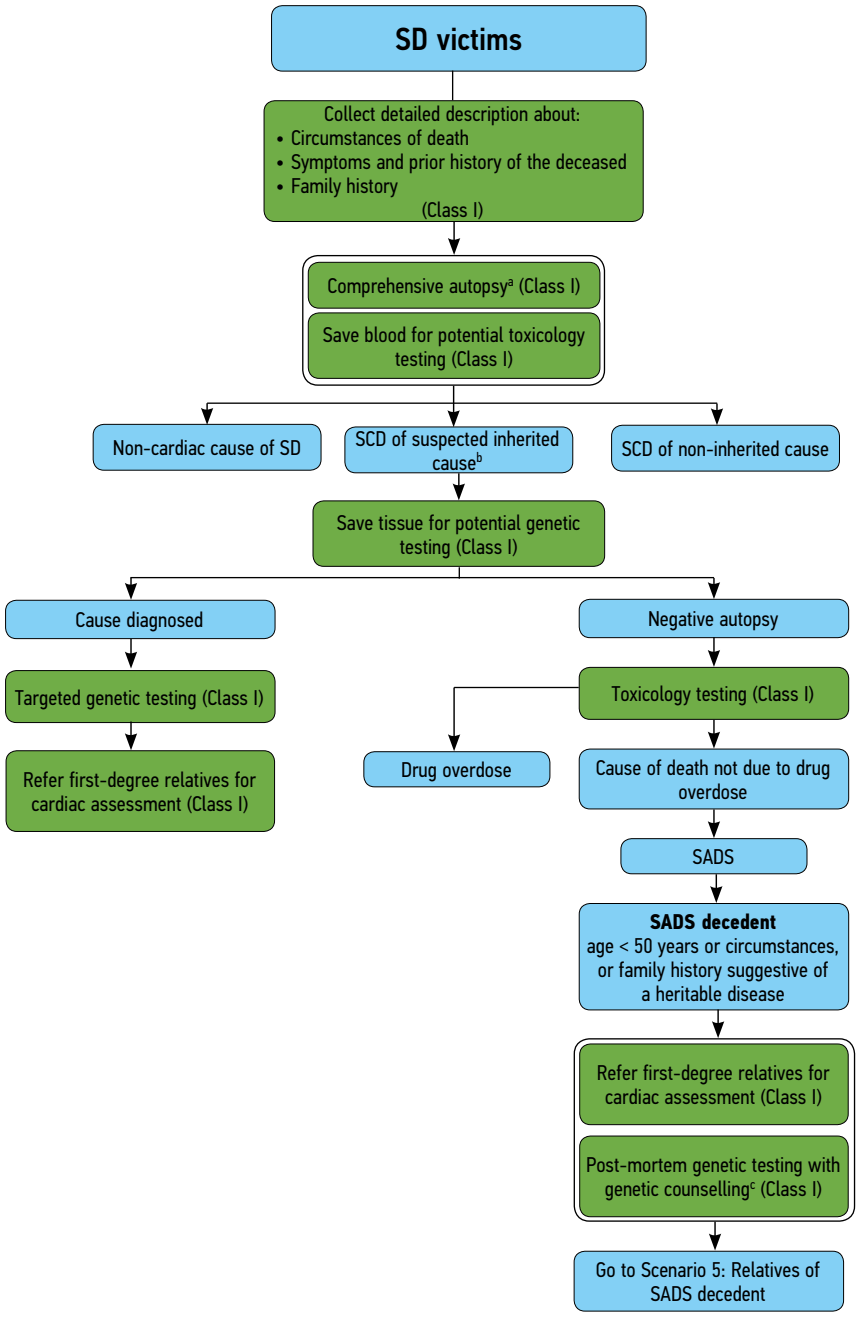

Fig 7. Algorithm for the evaluation of sudden death victims (adapted from the 2022 ESC Guidelines for the Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death) [1]. SADS, sudden arrhythmic death syndrome; SCD, sudden cardiac death; SD, sudden death.
[a]Autopsy is recommended, ideally in all cases of unexpected SD and always in those under 50 years. Autopsy should include full macroscopic examination and histopathology of all organs. The heart should ideally be examined by an expert cardiac pathologist. Samples suitable for DNA extraction should be retained when inherited causes or unexplained deaths are suspected. [b]Based on all circumstances, this includes negative autopsies, autopsies with uncertain findings, non-ischemic cardiomyopathies, coronary artery disease where familial hypercholesterolemia and thoracic aortic dissections are suspected. [c]After informed consent of relatives.

[42, 80, 84, 85]. Retaining tissue for DNA extraction is important for post-mortem genetic analysis, where the yield can be as high as one out of three [80, 83, 86].

Clinical evaluation and genetic testing of first-degree relatives is important if the cause of death after autopsy is unknown or suspected to be inherited.

Scenario 5: Relatives of SADS decedents

An algorithm for the evaluation of relatives of SADS decedents is presented in Figure 8.

Studies evaluating families of SADS decedents have identified underlying genetic heart disease in relatives that is presumed to be the cause of death in the absence of other findings. The overall diagnostic yield ranged from 18% to 53%, depending on population and clinical investigative protocols [87]. Etiologies included LQTS, BrS, CPVT, and other disorders, such as cardiomyopathy [87]. All study protocols relied upon a similar initial approach that involved evaluating the decedent's pathological reports, medical history, and manner of death, and then offering clinical evaluation to relatives with a minimum

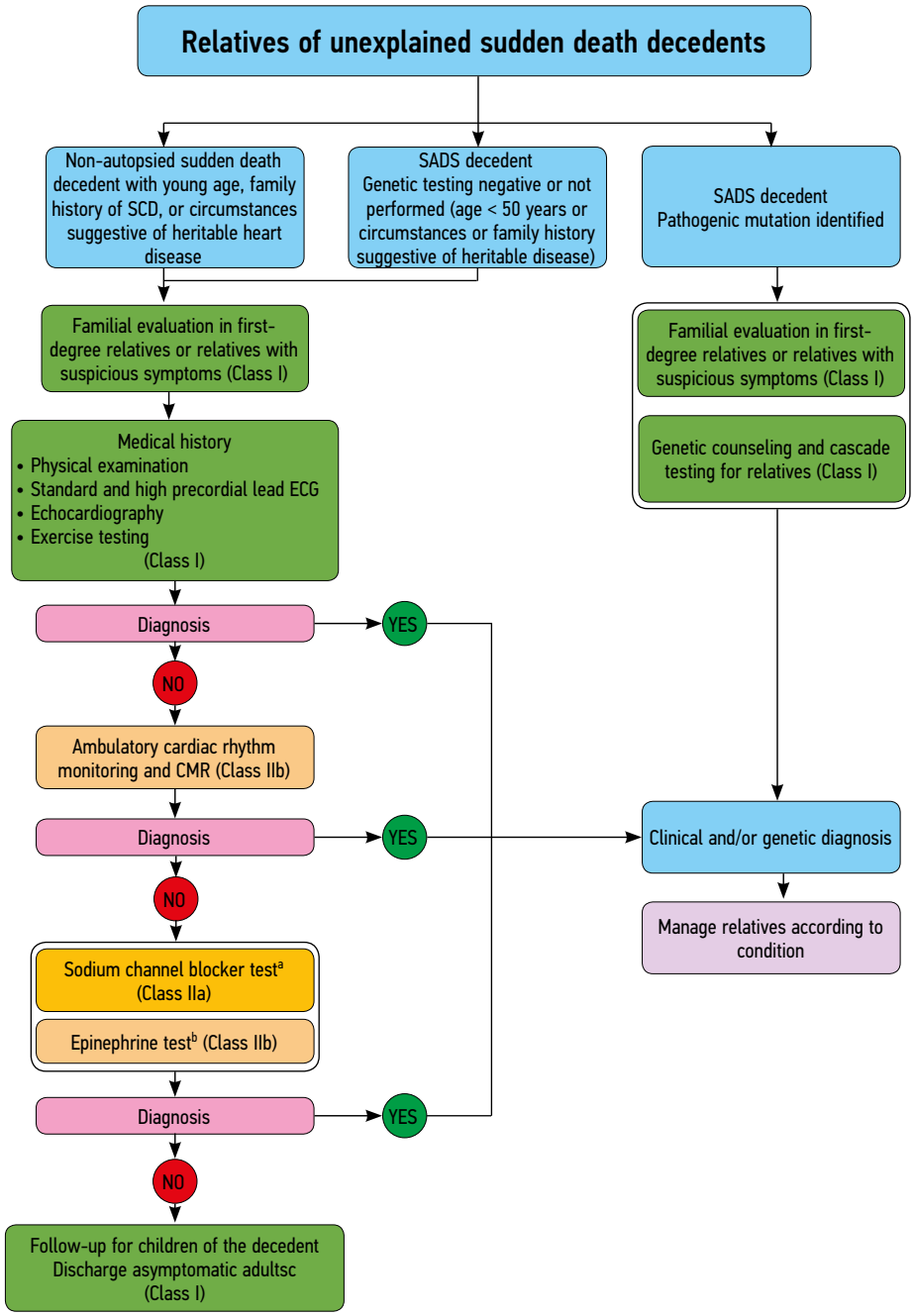

Fig. 8. Algorithm for the evaluation of relatives of unexplained sudden death decedents (adapted from the 2022 ESC Guidelines for the Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death) [1]. CMR, cardiac magnetic resonance; ECG, electrocardiogram; SADS, sudden arrhythmic death syndrome; SCD, sudden cardiac death.
[a] Over 16 years old ± any suspicions for BrS on tests or decedent circumstances of death. [b] If exercise is not feasible. [c] Re-evaluate if changes in family history or new symptoms.

of personal history, family history, physical examination, ECG and exercise test, and echocardiography [42, 85, 88–94]. The frequency of usage of additional tests, such as high lead ECGs, Holter monitoring, signal-averaged ECG, CMR, and provocative testing was where they diverged [95]. Routine follow-up of families without a diagnosis yields little in new diagnoses [96]. Even so, children of decedents may be monitored for age-penetrant disease until adulthood [97].

Reviews of other recommendation sections are scheduled for publication in future issues of the journal.

ADDITIONAL INFORMATION

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REFERENCES

1. 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

2. Faber TS, Gradinger R, Treusch S, et al. Incidence of ventricular tachyarrhythmias during permanent pacemaker therapy in low-risk patients results from the German multicentre EVENTS study. *Eur Heart J*. 2007;28(18):2238–2242. DOI: 10.1093/eurheartj/ehm242

3. Brignole M, Moya A, de Lange FJ, et al. 2018 ESC Guidelines for the diagnosis and management of syncope. *Eur Heart J*. 2018;39(21):1883–1948. DOI: 10.1093/eurheartj/ehy037

4. Middlekauff HR, Stevenson WG, Stevenson LW, Saxon LA. Syncope in advanced heart failure: high risk of sudden death regardless of origin of syncope. *J Am Coll Cardio*. 1993;21(1): 110–116. DOI: 10.1016/0735-1097(93)90724-f

5. Noda T, Shimizu W, Taguchi A, et al. Malignant entity of idiopathic ventricular fibrillation and polymorphic ventricular tachycardia initiated by premature extrasystoles originating from the right ventricular outflow tract. *J Am Coll Cardiol*. 2005;46(7):1288–1294. DOI: 10.1016/j.jacc.2005.05.077

6. Belhassen B, Viskin S. Idiopathic ventricular tachycardia and fibrillation. *J Cardiovasc Electrophysiol*. 1993;4(3):356–368. DOI: 10.1111/j.1540-8167.1993.tb01236.x

7. Zareba W, Platonov P. ECG patterns related to arrhythmias and sudden death: channelopathies, early repolarization, and pre-excitation. Camm JA, editor. *The ESC Textbook of Cardiovascular Medicine. 3 edn, The European Society of Cardiology Series*. Oxford: Oxford University Press, 2018. P. 382–389. DOI: 10.1093/med/9780198784906.003.0074

8. Binder T. Transthoracic echocardiography and the standard examination of specific cardiac structures. Camm JA, editor. *The ESC Textbook of Cardiovascular Medicine. 3 edn, The European Society of Cardiology Series*. Oxford: Oxford University Press, 2018. P. 426–431. DOI: 10.1093/med/9780198784906.003.0085

9. Voigt J-U. Left ventricular function, heart failure, and resynchronization therapy. Camm JA, editor. *The ESC Textbook of Cardiovascular Medicine. 3 edn, The European Society of Cardiology Series*. Oxford: Oxford University Press, 2018. P. 451–454. DOI: 10.1093/med/9780198784906.003.0092

10. Edvardsen T. Cardiomyopathies, myocarditis, and the transplanted heart. Camm JA, editor. *The ESC Textbook of Cardiovascular Medicine. 3 edn, The European Society of Cardiology Series*. Oxford: Oxford University Press, 2018. P. 456–460. DOI: 10.1093/med/9780198784906.003.0094_update_001

11. Cygankiewicz I. Ambulatory ECG monitoring. Camm JA, editor. *The ESC Textbook of Cardiovascular Medicine. 3 edn, The European Society of Cardiology Series*. Oxford: Oxford University Press, 2018. P. 393–400. DOI: 10.1093/med/9780198784906.003.0798

12. Gray B, Kirby A, Kabunga P, et al. Twelve-lead ambulatory electrocardiographic monitoring in Brugada syndrome: potential diagnostic and prognostic implications. *Heart Rhythm*. 2017;14(6):866–874. DOI: 10.1016/j.hrthm.2017.02.026

13. Karogiannis N, Senior R. Stress echocardiography. Camm JA, editor. *The ESC Textbook of Cardiovascular Medicine. 3 edn, The European Society of Cardiology Series*. Oxford: Oxford University Press, 2018. P. 432–434. DOI: 10.1093/med/9780198784906.003.0086_update_001

14. Di Marco A, Anguera I, Schmitt M, et al. Late gadolinium enhancement and the risk for ventricular arrhythmias or sudden death in dilated cardiomyopathy: systematic review and meta-analysis. *JACC Heart Fail*. 2017;5(1):28–38. DOI: 10.1016/j.jchf.2016.09.017

15. Josephson ME, Callans DJ. Using the twelve-lead electrocardiogram to localize the site of origin of ventricular tachycardia. *Heart Rhythm*. 2005;2(4):443–446. DOI: 10.1016/j.hrthm.2004.12.014

16. Nucifora G, Muser D, Masci PG, et al. Prevalence and prognostic value of concealed structural abnormalities in patients with apparently idiopathic ventricular arrhythmias of left versus right ventricular origin: a magnetic resonance imaging study. *Circ Arrhythm Electrophysiol*. 2014;7(3):456–462. DOI: 10.1161/CIRCEP.113.001172

17. Corrado D, Basso C, Leoni L, et al. Three-dimensional electroanatomic voltage mapping increases accuracy of diagnosing arrhythmogenic right ventricular cardiomyopathy/dysplasia. *Circulation*. 2005;111(23):3042–3050. DOI: 10.1161/CIRCULATIONAHA.104.486977

18. Casella M, Dello Russo A, Bergonti M, et al. Diagnostic yield of electroanatomic voltage mapping in guiding endomyocardial biopsies. *Circulation*. 2020;142(13):1249–1260. DOI: 10.1161/CIRCULATIONAHA.120.046900

19. Haanschoten DM, Adiyaman A, 't Hart NA, et al. Value of 3D mapping-guided endomyocardial biopsy in cardiac sarcoidosis: case series and narrative review on the value of electro-anatomic mapping-guided endomyocardial biopsies. *Eur J Clin Invest*. 2021;51(4):e13497. DOI: 10.1111/eci.13497

20. Tung R, Bauer B, Schelbert H, et al. Incidence of abnormal positron emission tomography in patients with unexplained cardiomyopathy and ventricular arrhythmias: the potential role of occult inflammation in arrhythmogenesis. *Heart Rhythm*. 2015;12(12):2488–2498. DOI: 10.1016/j.hrthm.2015.08.014

21. Palmisano A, Vignale D, Peretto G, et al. Hybrid FDG-PET/MR or FDG-PET/CT to detect disease activity in patients with persisting arrhythmias after myocarditis. *JACC Cardiovasc Imaging*. 2021;14(1):288–292. DOI: 10.1016/j.jcmg.2020.03.009

22. Dumas F, Geri G, Manzo-Silberman S, et al. Immediate percutaneous coronary intervention is associated with improved short- and long-term survival after out-of-hospital cardiac arrest. *Circ Cardiovasc Interv*. 2010;3(3):200–207. DOI: 10.1161/CIRCINTERVENTIONS.109.913665

23. Vyas A, Chan PS, Cram P, et al. Early coronary angiography and survival after out-of-hospital cardiac arrest. *Circ Cardiovasc Interv*. 2015;8(10):e002321. DOI: 10.1161/CIRCINTERVENTIONS.114.002321

24. Kalarus Z, Svendsen JH, Capodanno D, et al. Cardiac arrhythmias in the emergency settings of acute coronary syndrome and revascularization: an European Heart Rhythm Association (EHRA) consensus document, endorsed by the European Association of Percutaneous Cardiovascular Interventions (EAPCI), and European Acute Cardiovascular Care Association (ACCA). *Europace*. 2019;21(10):1603–1604. DOI: 10.1093/europace/euz163

25. Noc M, Fajadet J, Lassen JF, et al. Invasive coronary treatment strategies for out-of-hospital cardiac arrest: a consensus statement from the European association for percutaneous cardiovascular interventions (EAPCI)/stent for life (SFL) groups. *EuroIntervention*. 2014;10(1):31–37. DOI: 10.4244/EIJV10I1A7

26. Verma BR, Sharma V, Shekhar S, et al. Coronary angiography in patients with out-of-hospital cardiac arrest without ST-segment elevation: a systematic review and meta-analysis. *JACC Cardiovasc Interv*. 2020;13(19):2193–2205. DOI: 10.1016/j.jcin.2020.07.018

27. Barbarawi M, Zayed Y, Kheiri B, et al. Optimal timing of coronary intervention in patients resuscitated from cardiac arrest without ST-segment elevation myocardial infarction (NSTEMI): a systematic review and meta-analysis. *Resuscitation*. 2019;144:137–144. DOI: 10.1016/j.resuscitation.2019.06.279

28. Meng-Chang Y, Meng-Jun W, Xiao-Yan X, et al. Coronary angiography or not after cardiac arrest without ST segment elevation: a systematic review and meta-analysis. *Medicine (Baltimore)*. 2020;99(41):e22197. DOI: 10.1097/MD.0000000000022197

29. Khan MS, Shah SMM, Mubashir A, et al. Early coronary angiography in patients resuscitated from out of hospital cardiac arrest without ST-segment elevation: a systematic review and meta-analysis. *Resuscitation*. 2017;121:127–134. DOI: 10.1016/j.resuscitation.2017.10.019

30. Welsford M, Bossard M, Shortt C, et al. Does early coronary angiography improve survival after out-of-hospital cardiac arrest? A systematic review with meta-analysis. *Can J Cardiol*. 2018;34(2):80–194. DOI: 10.1016/j.cjca.2017.09.012

31. Chelly J, Mongardon N, Dumas F, et al. Benefit of an early and systematic imaging procedure after cardiac arrest: insights from the PROCAT (Parisian Region Out of Hospital Cardiac Arrest) registry. *Resuscitation*. 2012;83(12):1444–1450. DOI: 10.1016/j.resuscitation.2012.08.321

32. Stiles MK, Wilde AAM, Abrams DJ, et al. 2020 APHRS/HRS expert consensus statement on the investigation of decedents with sudden unexplained death and patients with sudden cardiac arrest, and of their families. *Heart Rhythm*. 2021;18(1):e1–e50. DOI: 10.1016/j.hrthm.2020.10.010

33. Tseng ZH, Olgin JE, Vittinghoff E, et al. Prospective countywide surveillance and autopsy characterization of sudden cardiac death: POST SCD study. *Circulation*. 2018;137(25):2689–2700. DOI: 10.1161/CIRCULATIONAHA.117.033427

34. Fellmann F, van El CG, Charron P, et al. European recommendations integrating genetic testing into multidisciplinary management of sudden cardiac death. *Eur J Hum Genet*. 2019;27:1763–1773. DOI: 10.1038/s41431-019-0445-y

35. Yamamoto T, Takayama M, Sato N, et al. Inappropriate analyses of automated external defibrillators used during in-hospital ventricular fibrillation. *Circ J*. 2008;72(4):679–681. DOI: 10.1253/circj.72.679

36. Sweeney MO, Ruetz LL, Belk P, et al. Bradycardia pacing-induced short-long-short sequences at the onset of ventricular tachyarrhythmias: a possible mechanism of proarrhythmia? *J Am Coll Cardiol*. 2007;50(7):614–622. DOI: 10.1016/j.jacc.2007.02.077

37. Tseng ZH, Hayward RM, Clark NM, et al. Sudden death in patients with cardiac implantable electronic devices. *JAMA Intern Med*. 2015;175(8):1342–1350. DOI: 10.1001/jamainternmed.2015.2641

38. Lacour P, Buschmann C, Storm C, et al. Cardiac implantable electronic device interrogation at forensic autopsy: an underestimated resource? *Circulation*. 2018;137(25):2730–2740. DOI: 10.1161/CIRCULATIONAHA.117.032367

39. Curcio A, Mazzanti A, Bloise R, et al. Clinical presentation and outcome of Brugada syndrome diagnosed with the new 2013 criteria. *J Cardiovasc Electrophysiol*. 2016;27(8):937–943. DOI: 10.1111/jce.12997

40. Haïssaguerre M, Shah DC, Jaïs P, et al. Role of Purkinje conducting system in triggering of idiopathic ventricular fibrillation. *Lancet*. 2002;359(9307):677–678. DOI: 10.1016/S0140-6736(02)07807-8

41. Krahn AD, Healey JS, Chauhan V, et al. Systematic assessment of patients with unexplained cardiac arrest: cardiac arrest survivors with preserved ejection fraction registry (CASPER). *Circulation*. 2009;120(4):278–285. DOI: 10.1161/CIRCULATIONAHA.109.853143

42. van der Werf C, Hofman N, Tan HL, et al. Diagnostic yield in sudden unexplained death and aborted cardiac arrest in the young: the experience of a tertiary referral center in The Netherlands. *Heart Rhythm*. 2010;7(10):1383–1389. DOI: 10.1016/j.hrthm.2010.05.036

43. Waldmann V, Karam N, Bougouin W, et al. Burden of coronary artery disease as a cause of sudden cardiac arrest in the young. *J Am Coll Cardiol*. 2019;73(16):2118–2120. DOI: 10.1016/j.jacc.2019.01.064

44. Eckart RE, Scoville SL, Campbell CL, et al. Sudden death in young adults: a 25-year review of autopsies in military recruits. *Ann Intern Med*. 2004;141(11):829–834. DOI: 10.7326/0003-4819-141-11-200412070-00005

45. Kunadian V, Chieffo A, Camici PG, et al. An EAPCI expert consensus document on ischaemia with non-obstructive coronary arteries in collaboration with European Society of Cardiology Working Group on Coronary Pathophysiology & Microcirculation Endorsed by Coronary Vasomotor Disorders International Study Group. *Eur Heart J*. 2021;16(13):1049–1069. DOI: 10.4244/EIJY20M07_01

46. Rodrigues P, Joshi A, Williams H, et al. Diagnosis and prognosis in sudden cardiac arrest survivors without coronary artery disease: utility of a clinical approach using cardiac magnetic resonance imaging. *Circ Cardiovasc Imaging*. 2017;10(12):e006709. DOI: 10.1161/CIRCIMAGING.117.006709

47. White JA, Fine NM, Gula L, et al. Utility of cardiovascular magnetic resonance in identifying substrate for malignant ventricular arrhythmias. *Circ Cardiovasc Imaging*. 2012;5(1):12–20. DOI: 10.1161/CIRCIMAGING.111.966085

48. Basso C, Perazzolo Marra M, Rizzo S, et al. Arrhythmic mitral valve prolapse and sudden cardiac death. *Circulation*. 2015;132(7):556–566. DOI: 10.1161/CIRCULATIONAHA.115.016291

49. Basso C, Iliceto S, Thiene G, Perazzolo Marra M. Mitral valve prolapse, ventricular arrhythmias, and sudden death. *Circulation*. 2019;140(11):952–964. DOI: 10.1161/CIRCULATIONAHA.118.034075

50. Govindan M, Batchvarov VN, Raju H, et al. Utility of high and standard right precordial leads during ajmaline testing for the diagnosis of Brugada syndrome. *Heart*. 2010;96(23):1904–1908. DOI: 10.1136/hrt.2010.201244

51. Obeyesekere MN, Klein GJ, Modi S, et al. How to perform and interpret provocative testing for the diagnosis of Brugada syndrome, long-QT syndrome, and catecholaminergic polymorphic ventricular tachycardia. *Circ Arrhythm Electrophysiol*. 2011;4(6):958–964. DOI: 10.1161/CIRCEP.111.965947

52. Cheung CC, Mellor G, Deyell MW, et al. Comparison of ajmaline and procainamide provocation tests in the diagnosis of Brugada syndrome. *JACC Clin Electrophysiol*. 2019;5(4):504–512. DOI: 10.1016/j.jacep.2019.01.026

53. Antzelevitch C, Yan G-X, Ackerman MJ, et al. J-Wave syndromes expert consensus conference report: emerging concepts and gaps in knowledge. *Europace*. 2016;32(5):315–339. DOI: 10.1016/j.joa.2016.07.002

54. Garratt CJ, Antoniou A, Griffith MJ, et al. Use of intravenous adenosine in sinus rhythm as a diagnostic test for latent preexcitation. *Am J Cardiol*. 1990;65(13):868–873. DOI: 10.1016/0002-9149(90)91428-9

55. Foo FS, Stiles MK, Heaven D. Unmasking latent preexcitation of a right-sided accessory pathway with intravenous adenosine after unexplained sudden cardiac arrest. *J Arrhythm*. 2020;36(5):939–941. DOI: 10.1002/joa3.12408

56. Krahn AD, Healey JS, Chauhan VS, et al. Epinephrine infusion in the evaluation of unexplained cardiac arrest and familial sudden death: from the cardiac arrest survivors with preserved Ejection Fraction Registry. *Circ Arrhythm Electrophysiol*. 2012;5(5):933–940. DOI: 10.1161/CIRCEP.112.973230

57. Denis A, Sacher F, Derval N, et al. Diagnostic value of isoproterenol testing in arrhythmogenic right ventricular cardiomyopathy. *Circ Arrhythm Electrophysiol*. 2014;7(4):590–597. DOI: 10.1161/CIRCEP.113.001224

58. Marjamaa A, Hiippala A, Arrhenius B, et al. Intravenous epinephrine infusion test in diagnosis of catecholaminergic polymorphic ventricular tachycardia. *J Cardiovasc Electrophysiol*. 2012;23(2):194–199. DOI: 10.1111/j.1540-8167.2011.02188.x

59. Ackerman MJ, Khositseth A, Tester DJ, et al. Epinephrine-induced QT interval prolongation: a gene-specific paradoxical response in congenital long QT syndrome. *Mayo Clin Proc*. 2002;77(5):413–421. DOI: 10.4065/77.5.413

60. Shimizu W, Noda T, Takaki H, et al. Diagnostic value of epinephrine test for genotyping LQT1, LQT2, and LQT3 forms of congenital long QT syndrome. *Heart Rhythm*. 2004;1(3):276–283. DOI: 10.1016/j.hrthm.2004.04.021

61. Magnano AR, Talathoti N, Hallur R, et al. Sympathomimetic infusion and cardiac repolarization: the normative effects of epinephrine and isoproterenol in healthy subjects. *J Cardiovasc Electrophysiol*. 2006;17(9):983–989. DOI: 10.1111/j.1540-8167.2006.00555.x

62. Vyas H, Hejlik J, Ackerman MJ. Epinephrine QT stress testing in the evaluation of congenital long-QT syndrome: diagnostic accuracy of the paradoxical QT response. *Circulation*. 2006;113(11):1385–1392. DOI: 10.1161/CIRCULATIONAHA.105.600445

63. Krahn AD, Healey JS, Chauhan V, et al. Systematic assessment of patients with unexplained cardiac arrest: cardiac arrest survivors with preserved ejection fraction registry (CASPER). *Circulation*. 2009;120(4):278–285. DOI: 10.1161/CIRCULATIONAHA.109.853143

64. Waldmann V, Bougouin W, Karam N, et al. Coronary vasospasm-related sudden cardiac arrest in the community. *J Am Coll Cardiol*. 2018;72(7):814–815. DOI: 10.1016/j.jacc.2018.05.051

65. Etienne P, Huchet F, Gaborit N, et al. Mental stress test: a rapid, simple, and efficient test to unmask long QT syndrome. *Europace*. 2018;20(12):2014–2020. DOI: 10.1093/europace/euy078

66. Kop WJ, Krantz DS, Nearing BD, et al. Effects of acute mental stress and exercise on T-wave alternans in patients with implantable cardioverter defibrillators and controls. *Circulation*. 2004;109(15):1864–1869. DOI: 10.1161/01.CIR.0000124726.72615.60

67. Marcus FI, McKenna WJ, Sherrill D, et al. Diagnosis of arrhythmogenic right ventricular cardiomyopathy/dysplasia: proposed modification of the task force criteria. *Eur Heart J*. 2010;31(7):806–814. DOI: 10.1093/eurheartj/ehq025

68. Giudicessi JR, Ackerman MJ. Exercise testing oversights underlie missed and delayed diagnosis of catecholaminergic polymorphic ventricular tachycardia in young sudden cardiac arrest survivors. *Heart Rhythm*. 2019;16(8):1232–1239. DOI: 10.1016/j.hrthm.2019.02.012

69. Sy RW, van der Werf C, Chattha IS, et al. Derivation and validation of a simple exercise-based algorithm for prediction of genetic testing in relatives of LQTS probands. *Circulation*. 2011;124(20):2187–2194. DOI: 10.1161/CIRCULATIONAHA.111.028258

70. Adler A, van der Werf C, Postema PG, et al. The phenomenon of 'QT stunning': the abnormal QT prolongation provoked by standing persists even as the heart rate returns to normal in patients with long QT syndrome. *Heart Rhythm*. 2012;9(6):901–908. DOI: 10.1016/j.hrthm.2012.01.026

71. Schwartz PJ, Lia C. QTc behavior during exercise and genetic testing for the long-QT syndrome. *Circulation*. 2011;124(20): 2181–2184. DOI: 10.1161/CIRCULATIONAHA.111.062182

72. Wang Y, Scheinman MM, Chien WW, et al. Patients with supraventricular tachycardia presenting with aborted sudden death: incidence, mechanism and long-term follow-up. *J Am Coll Cardiol*. 1991;18(7):1711–1719. DOI: 10.1016/0735-1097(91)90508-7

73. Roberts JD, Gollob MH, Young C, et al. Bundle branch reentrant ventricular tachycardia: novel genetic mechanisms in a lifethreatening arrhythmia. *JACC Clin Electrophysiol*. 2017;3(3): 276–288. DOI: 10.1016/j.jacep.2016.09.019

74. Santangeli P, Hamilton-Craig C, Dello Russo A, et al. Imaging of scar in patients with ventricular arrhythmias of right ventricular origin: cardiac magnetic resonance versus electroanatomic mapping. *J Cardiovasc Electrophysiol*. 2011;22(12):1359–1366. DOI: 10.1111/j.1540-8167.2011.02127.x

75. Haïssaguerre M, Duchateau J, Dubois R, et al. Idiopathic ventricular fibrillation: role of Purkinje system and microstructural myocardial abnormalities. *JACC Clin Electrophysiol*. 2020;6(6): 591–608. DOI: 10.1016/j.jacep.2020.03.010

76. Haïssaguerre M, Hocini M, Cheniti G, et al. Localized structural alterations underlying a subset of unexplained sudden cardiac death. *Circ Arrhythm Electrophysiol*. 2018;11(7):e006120. DOI: 10.1161/CIRCEP.117.006120

77. Mellor G, Laksman ZWM, Tadros R, et al. Genetic testing in the evaluation of unexplained cardiac arrest: from the CASPER (Cardiac Arrest Survivors With Preserved Ejection Fraction Registry). *Circ Cardiovasc Genet*. 2017;10(3):e001686. DOI: 10.1161/CIRCGENETICS.116.001686

78. Burns C, Bagnall RD, Lam L, et al. Multiple gene variants in hypertrophic cardiomyopathy in the era of next-generation sequencing. *Circ-Genom Precis Med*. 2017;10(4):e001666. DOI: 10.1161/CIRCGENETICS.116.001666

79. Winkel BG, Holst AG, Theilade J, et al. Nationwide study of sudden cardiac death in persons aged 1–35 years. *Eur Heart J*. 2011;32(8):983–990. DOI: 10.1093/eurheartj/ehq428

80. Bagnall RD, Weintraub RG, Ingles J, et al. A prospective study of sudden cardiac death among children and young adults. *N Engl J Med*. 2016;374:2441–2452. DOI: 10.1056/NEJMoa1510687

81. Winkel BG, Risgaard B, Sadjadieh G, et al. Sudden cardiac death in children (1–18 years): symptoms and causes of death in a nationwide setting. *Eur Heart J*. 2014;35(13):868–875. DOI: 10.1093/eurheartj/eht509

82. Risgaard B, Winkel BG, Jabbari R, et al. Burden of sudden cardiac death in persons aged 1 to 49 years: nationwide study in Denmark. *Circ Arrhythm Electrophysiol*. 2014;7(2):205–211. DOI: 10.1161/CIRCEP.113.001421

83. Hansen BL, Jacobsen EM, Kjerrumgaard A, et al. Diagnostic yield in victims of sudden cardiac death and their relatives. *Europace*. 2020;22(6):964–971. DOI: 10.1093/europace/euaa056

84. Lahrouchi N, Raju H, Lodder EM, et al. Utility of post-mortem genetic testing in cases of sudden arrhythmic death syndrome. *J Am Coll Cardiol*. 2017;69(17):2134–2145. DOI: 10.1016/j.jacc.2017.02.046

85. Tan HL, Hofman N, van Langen IM, et al. Sudden unexplained death: heritability and diagnostic yield of cardiological and genetic examination in surviving relatives. *Circulation*. 2005;112(2):207–213. DOI: 10.1161/CIRCULATIONAHA.104.522581

86. Lahrouchi N, Raju H, Lodder EM, et al. The yield of postmortem genetic testing in sudden death cases with structural findings at autopsy. *Eur J Hum Genet*. 2020;28:17–22. DOI: 10.1038/s41431-019-0500-8

87. Miles CJ, Behr ER. The role of genetic testing in unexplained sudden death. *Transl Res*. 2016;168:59–73. DOI: 10.1016/j.trsl.2015.06.007

88. Behr E, Wood DA, Wright M, et al. Cardiological assessment of first-degree relatives in sudden arrhythmic death syndrome. *Lancet*. 2003;362(9394):1457–1459. DOI: 10.1016/s0140-6736(03)14692-2

89. Behr ER, Dalageorgou C, Christiansen M, et al. Sudden arrhythmic death syndrome: familial evaluation identifies inheritable heart disease in the majority of families. *Eur Heart J*. 2008;29(13): 1670–1680. DOI: 10.1093/eurheartj/ehn219

90. Kumar S, Peters S, Thompson T, et al. Familial cardiological and targeted genetic evaluation: low yield in sudden unexplained death and high yield in unexplained cardiac arrest syndromes. *Heart Rhythm*. 2013;10(11):1653–1660. DOI: 10.1016/j.hrthm.2013.08.022

91. McGorrian C, Constant O, Harper N, et al. Family-based cardiac screening in relatives of victims of sudden arrhythmic death syndrome. *Europace*. 2013;15(7):1050–1058. DOI: 10.1093/europace/eus408

92. Mellor G, Raju H, de Noronha SV, et al. Clinical characteristics and circumstances of death in the sudden arrhythmic death syndrome. *Circ Arrhythm Electrophysiol*. 2014;7(6):1078–1083. DOI: 10.1161/CIRCEP.114.001854

93. Papadakis M, Papatheodorou E, Mellor G, et al. The diagnostic yield of Brugada syndrome after sudden death with normal autopsy. *J Am Coll Cardiol*. 2018;71(11):1204–1214. DOI: 10.1016/j.jacc.2018.01.031

94. Mellor G, Nelson CP, Robb C, et al. The prevalence and significance of the early repolarization pattern in sudden arrhythmic death syndrome families. *Circ Arrhythm Electrophysiol*. 2016;9(6):e003960. DOI: 10.1161/CIRCEP.116.003960

95. Priori SG, Wilde AA, Horie M, et al. Executive summary: HRS/EHRA/APHRS expert consensus statement on the diagnosis and management of patients with inherited primary arrhythmia syndromes. *Europace*. 2013;15(10):1389–1406. DOI: 10.1093/europace/eut272

96. van der Werf C, Stiekema L, Tan HL, et al. Low rate of cardiac events in first-degree relatives of diagnosis-negative young sudden unexplained death syndrome victims during follow-up. *Heart Rhythm*. 2014;11(10):1728–1732. DOI: 10.1016/j.hrthm.2014.05.028

97. Wong LCH, Roses-Noguer F, Till JA, Behr ER. Cardiac evaluation of pediatric relatives in sudden arrhythmic death syndrome: a 2-center experience. *Circ Arrhythm Electrophysiol*. 2014;7(5): 800–806. DOI: 10.1161/CIRCEP.114.001818

СПИСОК ЛИТЕРАТУРЫ

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

2. Faber T.S., Gradinger R., Treusch S., et al. Incidence of ventricular tachyarrhythmias during permanent pacemaker therapy in low-risk patients results from the German multicentre EVENTS study // Eur Heart J. 2007. Vol. 28, No. 18. P. 2238–2242. DOI: 10.1093/eurheartj/ehm242

3. Brignole M., Moya A., de Lange F.J., et al. 2018 ESC Guidelines for the diagnosis and management of syncope // Eur Heart J. 2018. Vol. 39, No. 21. P. 1883–1948. DOI: 10.1093/eurheartj/ehy037

4. Middlekauff H.R., Stevenson W.G., Stevenson L.W., Saxon L.A. Syncope in advanced heart failure: high risk of sudden death regardless of origin of syncope // J Am Coll Cardio. 1993. Vol. 21, No. 1. P. 110–116. DOI: 10.1016/0735-1097(93)90724-f

5. Noda T., Shimizu W., Taguchi A., et al. Malignant entity of idiopathic ventricular fibrillation and polymorphic ventricular tachycardia initiated by premature extrasystoles originating from the right ventricular outflow tract // J Am Coll Cardiol. 2005. Vol. 46, No. 7. P. 1288–1294. DOI: 10.1016/j.jacc.2005.05.077

6. Belhassen B., Viskin S. Idiopathic ventricular tachycardia and fibrillation // J Cardiovasc Electrophysiol. 1993. Vol. 4, No. 3. P. 356–368. DOI: 10.1111/j.1540-8167.1993.tb01236.x

7. Zareba W., Platonov P. ECG patterns related to arrhythmias and sudden death: channelopathies, early repolarization, and pre-excitation. The ESC Textbook of Cardiovascular Medicine. 3 edn, The European Society of Cardiology Series / J.A. Camm, editor. Oxford: Oxford University Press, 2018. P. 382–389. DOI: 10.1093/med/9780198784906.003.0074

8. Binder T. Transthoracic echocardiography and the standard examination of specific cardiac structures. The ESC Textbook of Cardiovascular Medicine. 3 edn, The European Society of Cardiology Series / J.A. Camm, editor. Oxford: Oxford University Press, 2018. P. 426–431. DOI: 10.1093/med/9780198784906.003.0085

9. Voigt J.-U. Left ventricular function, heart failure, and resynchronization therapy. The ESC Textbook of Cardiovascular Medicine. 3 edn, The European Society of Cardiology Series / J.A. Camm, editor. Oxford: Oxford University Press, 2018. P. 451–454. DOI: 10.1093/med/9780198784906.003.0092

10. Edvardsen T. Cardiomyopathies, myocarditis, and the transplanted heart. The ESC Textbook of Cardiovascular Medicine. 3 edn, The European Society of Cardiology Series / J.A. Camm, editor. Oxford: Oxford University Press, 2018. P. 456–460. DOI: 10.1093/med/9780198784906.003.0094_update_001

11. Cygankiewicz I. Ambulatory ECG monitoring. The ESC Textbook of Cardiovascular Medicine. 3 edn, The European Society of Cardiology Series / J.A. Camm, editor. Oxford: Oxford University Press, 2018. P. 393–400. DOI: 10.1093/med/9780198784906.003.0798

12. Gray B., Kirby A., Kabunga P., et al. Twelve-lead ambulatory electrocardiographic monitoring in Brugada syndrome: potential diagnostic and prognostic implications // Heart Rhythm. 2017. Vol. 14, No. 6. P. 866–874. DOI: 10.1016/j.hrthm.2017.02.026

13. Karogiannis N., Senior R. Stress echocardiography. The ESC Textbook of Cardiovascular Medicine. 3 edn, The European Society of Cardiology Series / J.A. Camm, editor. Oxford: Oxford University Press, 2018. P. 432–434. DOI: 10.1093/med/9780198784906.003.0086_update_001

14. Di Marco A., Anguera I., Schmitt M., et al. Late gadolinium enhancement and the risk for ventricular arrhythmias or sudden death in dilated cardiomyopathy: systematic review and meta-analysis // JACC Heart Fail. 2017. Vol. 5, No. 1. P. 28–38. DOI: 10.1016/j.jchf.2016.09.017

15. Josephson M.E., Callans D.J. Using the twelve-lead electrocardiogram to localize the site of origin of ventricular tachycardia // Heart Rhythm. 2005. Vol. 2, No. 4. P. 443–446. DOI: 10.1016/j.hrthm.2004.12.014

16. Nucifora G., Muser D., Masci P.G., et al. Prevalence and prognostic value of concealed structural abnormalities in patients with apparently idiopathic ventricular arrhythmias of left versus right ventricular origin: a magnetic resonance imaging study // Circ Arrhythm Electrophysiol. 2014. Vol. 7, No. 3. P. 456–462. DOI: 10.1161/CIRCEP.113.001172

17. Corrado D., Basso C., Leoni L., et al. Three-dimensional electroanatomic voltage mapping increases accuracy of diagnosing arrhythmogenic right ventricular cardiomyopathy/dysplasia // Circulation. 2005. Vol. 111, No. 23. P. 3042–3050. DOI: 10.1161/CIRCULATIONAHA.104.486977

18. Casella M., Dello Russo A., Bergonti M., et al. Diagnostic yield of electroanatomic voltage mapping in guiding endomyocardial

biopsies // Circulation. 2020. Vol. 142, No. 13. P. 1249–1260. DOI: 10.1161/CIRCULATIONAHA.120.046900

19. Haanschoten D.M., Adiyaman A., 't Hart N.A., et al. Value of 3D mapping-guided endomyocardial biopsy in cardiac sarcoidosis: case series and narrative review on the value of electro-anatomic mapping-guided endomyocardial biopsies // Eur J Clin Invest. 2021. Vol. 51, No. 4. ID e13497. DOI: 10.1111/eci.13497

20. Tung R., Bauer B., Schelbert H., et al. Incidence of abnormal positron emission tomography in patients with unexplained cardiomyopathy and ventricular arrhythmias: the potential role of occult inflammation in arrhythmogenesis // Heart Rhythm. 2015. Vol. 12, No. 12. P. 2488–2498. DOI: 10.1016/j.hrthm.2015.08.014

21. Palmisano A., Vignale D., Peretto G., et al. Hybrid FDG-PET/MR or FDG-PET/CT to detect disease activity in patients with persisting arrhythmias after myocarditis // JACC Cardiovasc Imaging. 2021. Vol. 14, No. 1. P. 288–292. DOI: 10.1016/j.jcmg.2020.03.009

22. Dumas F., Geri G., Manzo-Silberman S., et al. Immediate percutaneous coronary intervention is associated with improved short- and long-term survival after out-of-hospital cardiac arrest // Circ Cardiovasc Interv. 2010. Vol. 3, No. 3. P. 200–207. DOI: 10.1161/CIRCINTERVENTIONS.109.913665

23. Vyas A., Chan P.S., Cram P., et al. Early coronary angiography and survival after out-of-hospital cardiac arrest // Circ Cardiovasc Interv. 2015. Vol. 8, No. 10. ID e002321. DOI: 10.1161/CIRCINTERVENTIONS.114.002321

24. Kalarus Z., Svendsen J.H., Capodanno D., et al. Cardiac arrhythmias in the emergency settings of acute coronary syndrome and revascularization: an European Heart Rhythm Association (EHRA) consensus document, endorsed by the European Association of Percutaneous Cardiovascular Interventions (EAPCI), and European Acute Cardiovascular Care Association (ACCA) // Europace. 2019. Vol. 21, No. 10. P. 1603–1604. DOI: 10.1093/europace/euz163

25. Noc M., Fajadet J., Lassen J.F., et al. Invasive coronary treatment strategies for out-of-hospital cardiac arrest: a consensus statement from the European association for percutaneous cardiovascular interventions (EAPCI)/stent for life (SFL) groups // EuroIntervention. 2014. Vol. 10, No. 1. P. 31–37. DOI: 10.4244/EIJV10I1A7

26. Verma B.R., Sharma V., Shekhar S., et al. Coronary angiography in patients with out-of-hospital cardiac arrest without ST-segment elevation: a systematic review and meta-analysis // JACC Cardiovasc Interv. 2020. Vol. 13, No. 19. P. 2193–2205. DOI: 10.1016/j.jcin.2020.07.018

27. Barbarawi M., Zayed Y., Kheiri B., et al. Optimal timing of coronary intervention in patients resuscitated from cardiac arrest without ST-segment elevation myocardial infarction (NSTEMI): a systematic review and meta-analysis // Resuscitation. 2019. Vol. 144. P. 137–144. DOI: 10.1016/j.resuscitation.2019.06.279

28. Meng-Chang Y., Meng-Jun W., Xiao-Yan X., et al. Coronary angiography or not after cardiac arrest without ST segment elevation: a systematic review and meta-analysis // Medicine (Baltimore). 2020. Vol. 99, No. 41. ID e22197. DOI: 10.1097/MD.0000000000022197

29. Khan M.S., Shah S.M.M., Mubashir A., et al. Early coronary angiography in patients resuscitated from out of hospital cardiac arrest without ST-segment elevation: a systematic review and meta-analysis // Resuscitation. 2017. Vol. 121. P. 127–134. DOI: 10.1016/j.resuscitation.2017.10.019

30. Welsford M., Bossard M., Shortt C., et al. Does early coronary angiography improve survival after out-of-hospital cardiac arrest? A systematic review with meta-analysis // Can J Cardiol. 2018. Vol. 34, No. 2. P. 80–194. DOI: 10.1016/j.cjca.2017.09.012

31. Chelly J., Mongardon N., Dumas F., et al. Benefit of an early and systematic imaging procedure after cardiac arrest: insights from the PROCAT (Parisian Region Out of Hospital Cardiac Arrest) registry // Resuscitation. 2012. Vol. 83, No. 12. P. 1444–1450. DOI: 10.1016/j.resuscitation.2012.08.321

32. Stiles M.K., Wilde A.A.M., Abrams D.J., et al. 2020 APHRS/HRS expert consensus statement on the investigation of decedents with sudden unexplained death and patients with sudden cardiac arrest, and of their families // Heart Rhythm. 2021. Vol. 18, No. 1. P. e1–e50. DOI: 10.1016/j.hrthm.2020.10.010

33. Tseng Z.H., Olgin J.E., Vittinghoff E., et al. Prospective countywide surveillance and autopsy characterization of sudden cardiac death: POST SCD study // Circulation. 2018. Vol. 137, No. 25. P. 2689–2700. DOI: 10.1161/CIRCULATIONAHA.117.033427

34. Fellmann F., van El C.G., Charron P., et al. European recommendations integrating genetic testing into multidisciplinary management of sudden cardiac death // Eur J Hum Genet. 2019. Vol. 27. P. 1763–1773. DOI: 10.1038/s41431-019-0445-y

35. Yamamoto T., Takayama M., Sato N., et al. Inappropriate analyses of automated external defibrillators used during in-hospital ventricular fibrillation // Circ J. 2008. Vol. 72, No. 4. P. 679–681. DOI: 10.1253/circj.72.679

36. Sweeney M.O., Ruetz L.L., Belk P., et al. Bradycardia pacing-induced short-long-short sequences at the onset of ventricular tachyarrhythmias: a possible mechanism of proarrhythmia? // J Am Coll Cardiol. 2007. Vol. 50, No. 7. P. 614–622. DOI: 10.1016/j.jacc.2007.02.077

37. Tseng Z.H., Hayward R.M., Clark N.M., et al. Sudden death in patients with cardiac implantable electronic devices // JAMA Intern Med. 2015. Vol. 175, No. 8. P. 1342–1350. DOI: 10.1001/jamainternmed.2015.2641

38. Lacour P., Buschmann C., Storm C., et al. Cardiac implantable electronic device interrogation at forensic autopsy: an underestimated resource? // Circulation. 2018. Vol. 137, No. 25. P. 2730–2740. DOI: 10.1161/CIRCULATIONAHA.117.032367

39. Curcio A., Mazzanti A., Bloise R., et al. Clinical presentation and outcome of Brugada syndrome diagnosed with the new 2013 criteria // J Cardiovasc Electrophysiol. 2016. Vol. 27, No. 8. P. 937–943. DOI: 10.1111/jce.12997

40. Haïssaguerre M., Shah D.C., Jaïs P., et al. Role of Purkinje conducting system in triggering of idiopathic ventricular fibrillation // Lancet. 2002. Vol. 359, No. 9307. P. 677–678. DOI: 10.1016/S0140-6736(02)07807-8

41. Krahn A.D., Healey J.S., Chauhan V., et al. Systematic assessment of patients with unexplained cardiac arrest: cardiac arrest survivors with preserved ejection fraction registry

(CASPER) // Circulation. 2009. Vol. 120, No. 4. P. 278–285. DOI: 10.1161/CIRCULATIONAHA.109.853143

42. van der Werf C., Hofman N., Tan H.L., et al. Diagnostic yield in sudden unexplained death and aborted cardiac arrest in the young: the experience of a tertiary referral center in The Netherlands // Heart Rhythm. 2010. Vol. 7, No. 10. P. 1383–1389. DOI: 10.1016/j.hrthm.2010.05.036

43. Waldmann V., Karam N., Bougouin W., et al. Burden of coronary artery disease as a cause of sudden cardiac arrest in the young // J Am Coll Cardiol. 2019. Vol. 73, No. 16. P. 2118–2120. DOI: 10.1016/j.jacc.2019.01.064

44. Eckart R.E., Scoville S.L., Campbell C.L., et al. Sudden death in young adults: a 25-year review of autopsies in military recruits // Ann Intern Med. 2004. Vol. 141, No. 11. P. 829–834. DOI: 10.7326/0003-4819-141-11-200412070-00005

45. Kunadian V., Chieffo A., Camici P.G., et al. An EAPCI expert consensus document on ischaemia with non-obstructive coronary arteries in collaboration with European Society of Cardiology Working Group on Coronary Pathophysiology & Microcirculation Endorsed by Coronary Vasomotor Disorders International Study Group // Eur Heart J. 2021. Vol. 16, No. 13. P. 1049–1069. DOI: 10.4244/EIJY20M07_01

46. Rodrigues P., Joshi A., Williams H., et al. Diagnosis and prognosis in sudden cardiac arrest survivors without coronary artery disease: utility of a clinical approach using cardiac magnetic resonance imaging // Circ Cardiovasc Imaging. 2017. Vol. 10, No. 12. ID e006709. DOI: 10.1161/CIRCIMAGING.117.006709

47. White J.A., Fine N.M., Gula L., et al. Utility of cardiovascular magnetic resonance in identifying substrate for malignant ventricular arrhythmias // Circ Cardiovasc Imaging. 2012. Vol. 5, No. 1. P. 12–20. DOI: 10.1161/CIRCIMAGING.111.966085

48. Basso C., Perazzolo Marra M., Rizzo S., et al. Arrhythmic mitral valve prolapse and sudden cardiac death // Circulation. 2015. Vol. 132, No. 7. P. 556–566. DOI: 10.1161/CIRCULATIONAHA.115.016291

49. Basso C., Iliceto S., Thiene G., Perazzolo Marra M. Mitral valve prolapse, ventricular arrhythmias, and sudden death // Circulation. 2019. Vol. 140, No. 11. P. 952–964. DOI: 10.1161/CIRCULATIONAHA.118.034075

50. Govindan M., Batchvarov V.N., Raju H., et al. Utility of high and standard right precordial leads during ajmaline testing for the diagnosis of Brugada syndrome // Heart. 2010. Vol. 96, No. 23. P. 1904–1908. DOI: 10.1136/hrt.2010.201244

51. Obeyesekere M.N., Klein G.J., Modi S., et al. How to perform and interpret provocative testing for the diagnosis of Brugada syndrome, long-QT syndrome, and catecholaminergic polymorphic ventricular tachycardia // Circ Arrhythm Electrophysiol. 2011. Vol. 4, No. 6. P. 958–964. DOI: 10.1161/CIRCEP.111.965947

52. Cheung C.C., Mellor G., Deyell M.W., et al. Comparison of ajmaline and procainamide provocation tests in the diagnosis of Brugada syndrome // JACC Clin Electrophysiol. 2019. Vol. 5, No. 4. P. 504–512. DOI: 10.1016/j.jacep.2019.01.026

53. Antzelevitch C., Yan G.-X., Ackerman M.J., et al. J-Wave syndromes expert consensus conference report: emerging concepts and gaps in knowledge // Europace. 2016. Vol. 32, No. 5. P. 315–339. DOI: 10.1016/j.joa.2016.07.002

54. Garratt C.J., Antoniou A., Griffith M.J., et al. Use of intravenous adenosine in sinus rhythm as a diagnostic test for latent preexcitation // Am J Cardiol. 1990. Vol. 65, No. 13. P. 868–873. DOI: 10.1016/0002-9149(90)91428-9

55. Foo F.S., Stiles M.K., Heaven D. Unmasking latent preexcitation of a right-sided accessory pathway with intravenous adenosine after unexplained sudden cardiac arrest // J Arrhythm. 2020. Vol. 36, No. 5. P. 939–941. DOI: 10.1002/joa3.12408

56. Krahn A.D., Healey J.S., Chauhan V.S., et al. Epinephrine infusion in the evaluation of unexplained cardiac arrest and familial sudden death: from the cardiac arrest survivors with preserved Ejection Fraction Registry // Circ Arrhythm Electrophysiol. 2012. Vol. 5, No. 5. P. 933–940. DOI: 10.1161/CIRCEP.112.973230

57. Denis A., Sacher F., Derval N., et al. Diagnostic value of isoproterenol testing in arrhythmogenic right ventricular cardiomyopathy // Circ Arrhythm Electrophysiol. 2014. Vol. 7, No. 4. P. 590–597. DOI: 10.1161/CIRCEP.113.001224

58. Marjamaa A., Hiippala A., Arrhenius B., et al. Intravenous epinephrine infusion test in diagnosis of catecholaminergic polymorphic ventricular tachycardia // J Cardiovasc Electrophysiol. 2012. Vol. 23, No. 2. P. 194–199. DOI: 10.1111/j.1540-8167.2011.02188.x

59. Ackerman M.J., Khositseth A., Tester D.J., et al. Epinephrine-induced QT interval prolongation: a gene-specific paradoxical response in congenital long QT syndrome // Mayo Clin Proc. 2002. Vol. 77, No. 5. P. 413–421. DOI: 10.4065/77.5.413

60. Shimizu W., Noda T., Takaki H., et al. Diagnostic value of epinephrine test for genotyping LQT1, LQT2, and LQT3 forms of congenital long QT syndrome // Heart Rhythm. 2004. Vol. 1, No. 3. P. 276–283. DOI: 10.1016/j.hrthm.2004.04.021

61. Magnano A.R., Talathoti N., Hallur R., et al. Sympathomimetic infusion and cardiac repolarization: the normative effects of epinephrine and isoproterenol in healthy subjects // J Cardiovasc Electrophysiol. 2006. Vol. 17, No. 9. P. 983–989. DOI: 10.1111/j.1540-8167.2006.00555.x

62. Vyas H., Hejlik J., Ackerman M.J. Epinephrine QT stress testing in the evaluation of congenital long-QT syndrome: diagnostic accuracy of the paradoxical QT response // Circulation. 2006. Vol. 113, No. 11. P. 1385–1392. DOI: 10.1161/CIRCULATIONAHA.105.600445

63. Krahn A.D., Healey J.S., Chauhan V., et al. Systematic assessment of patients with unexplained cardiac arrest: cardiac arrest survivors with preserved ejection fraction registry (CASPER) // Circulation. 2009. Vol. 120, No. 4. P. 278–285. DOI: 10.1161/CIRCULATIONAHA.109.853143

64. Waldmann V., Bougouin W., Karam N., et al. Coronary vasospasm-related sudden cardiac arrest in the community // J Am Coll Cardiol. 2018. Vol. 72, No. 7. P. 814–815. DOI: 10.1016/j.jacc.2018.05.051

65. Etienne P., Huchet F., Gaborit N., et al. Mental stress test: a rapid, simple, and efficient test to unmask long QT syndrome // Europace. 2018. Vol. 20, No. 12. P. 2014–2020. DOI: 10.1093/europace/euy078

66. Kop W.J., Krantz D.S., Nearing B.D., et al. Effects of acute mental stress and exercise on T-wave alternans in patients with implantable cardioverter defibrillators and controls // Circulation. 2004. Vol. 109, No. 15. P. 1864–1869. DOI: 10.1161/01.CIR.0000124726.72615.60

67. Marcus F.I., McKenna W.J., Sherrill D., et al. Diagnosis of arrhythmogenic right ventricular cardiomyopathy/dysplasia: proposed modification of the task force criteria // Eur Heart J. 2010. Vol. 31, No. 7. P. 806–814. DOI: 10.1093/eurheartj/ehq025

68. Giudicessi J.R., Ackerman M.J. Exercise testing oversights underlie missed and delayed diagnosis of catecholaminergic polymorphic ventricular tachycardia in young sudden cardiac arrest survivors // Heart Rhythm. 2019. Vol. 16, No. 8. P. 1232–1239. DOI: 10.1016/j.hrthm.2019.02.012

69. Sy R.W., van der Werf C., Chattha I.S., et al. Derivation and validation of a simple exercise-based algorithm for prediction of genetic testing in relatives of LQTS probands // Circulation. 2011. Vol. 124, No. 20. P. 2187–2194. DOI: 10.1161/CIRCULATIONAHA.111.028258

70. Adler A., van der Werf C., Postema P.G., et al. The phenomenon of 'QT stunning': the abnormal QT prolongation provoked by standing persists even as the heart rate returns to normal in patients with long QT syndrome // Heart Rhythm. 2012. Vol. 9, No. 6. P. 901–908. DOI: 10.1016/j.hrthm.2012.01.026

71. Schwartz P.J., Lia C. QTc behavior during exercise and genetic testing for the long-QT syndrome // Circulation. 2011. Vol. 124, No. 20. P. 2181–2184. DOI: 10.1161/CIRCULATIONAHA.111.062182

72. Wang Y., Scheinman M.M., Chien W.W., et al. Patients with supraventricular tachycardia presenting with aborted sudden death: incidence, mechanism and long-term follow-up // J Am Coll Cardiol. 1991. Vol. 18, No. 7. P. 1711–1719. DOI: 10.1016/0735-1097(91)90508-7

73. Roberts J.D., Gollob M.H., Young C., et al. Bundle branch re-entrant ventricular tachycardia: novel genetic mechanisms in a lifethreatening arrhythmia // JACC Clin Electrophysiol. 2017. Vol. 3, No. 3. P. 276–288. DOI: 10.1016/j.jacep.2016.09.019

74. Santangeli P., Hamilton-Craig C., Dello Russo A., et al. Imaging of scar in patients with ventricular arrhythmias of right ventricular origin: cardiac magnetic resonance versus electroanatomic mapping // J Cardiovasc Electrophysiol. 2011. Vol. 22, No. 12. P. 1359–1366. DOI: 10.1111/j.1540-8167.2011.02127.x

75. Haïssaguerre M., Duchateau J., Dubois R., et al. Idiopathic ventricular fibrillation: role of Purkinje system and microstructural myocardial abnormalities // JACC Clin Electrophysiol. 2020. Vol. 6, No. 6. P. 591–608. DOI: 10.1016/j.jacep.2020.03.010

76. Haïssaguerre M., Hocini M., Cheniti G., et al. Localized structural alterations underlying a subset of unexplained sudden cardiac death // Circ Arrhythm Electrophysiol. 2018. Vol. 11, No. 7. ID e006120. DOI: 10.1161/CIRCEP.117.006120

77. Mellor G., Laksman Z.W.M., Tadros R., et al. Genetic testing in the evaluation of unexplained cardiac arrest: from the CASPER (Cardiac Arrest Survivors With Preserved Ejection Fraction Registry) // Circ Cardiovasc Genet. 2017. Vol. 10, No. 3. ID e001686. DOI: 10.1161/CIRCGENETICS.116.001686

78. Burns C., Bagnall R.D., Lam L., et al. Multiple gene variants in hypertrophic cardiomyopathy in the era of next-generation sequencing // Circ-Genom Precis Med. 2017. Vol. 10, No. 4. ID e001666. DOI: 10.1161/CIRCGENETICS.116.001666

79. Winkel B.G., Holst A.G., Theilade J., et al. Nationwide study of sudden cardiac death in persons aged 1–35 years // Eur Heart J. 2011. Vol. 32, No. 8. P. 983–990. DOI: 10.1093/eurheartj/ehq428

80. Bagnall R.D., Weintraub R.G., Ingles J., et al. A prospective study of sudden cardiac death among children and young adults // N Engl J Med. 2016. Vol. 374. P. 2441–2452. DOI: 10.1056/NEJMoa1510687

81. Winkel B.G., Risgaard B., Sadjadieh G., et al. Sudden cardiac death in children (1–18 years): symptoms and causes of death in a nationwide setting // Eur Heart J. 2014. Vol. 35, No. 13. P. 868–875. DOI: 10.1093/eurheartj/eht509

82. Risgaard B., Winkel B.G., Jabbari R., et al. Burden of sudden cardiac death in persons aged 1 to 49 years: nationwide study in Denmark // Circ Arrhythm Electrophysiol. 2014. Vol. 7, No. 2. P. 205–211. DOI: 10.1161/CIRCEP.113.001421

83. Hansen B.L., Jacobsen E.M., Kjerrumgaard A., et al. Diagnostic yield in victims of sudden cardiac death and their relatives // Europace. 2020. Vol. 22, No. 6. P. 964–971. DOI: 10.1093/europace/euaa056

84. Lahrouchi N., Raju H., Lodder E.M., et al. Utility of post-mortem genetic testing in cases of sudden arrhythmic death syndrome // J Am Coll Cardiol. 2017. Vol. 69, No. 17. P. 2134–2145. DOI: 10.1016/j.jacc.2017.02.046

85. Tan H.L., Hofman N., van Langen I.M., et al. Sudden unexplained death: heritability and diagnostic yield of cardiological and genetic examination in surviving relatives // Circulation. 2005. Vol. 112, No. 2. P. 207–213. DOI: 10.1161/CIRCULATIONAHA.104.522581

86. Lahrouchi N., Raju H., Lodder E.M., et al. The yield of postmortem genetic testing in sudden death cases with structural findings at autopsy // Eur J Hum Genet. 2020. Vol. 28. P. 17–22. DOI: 10.1038/s41431-019-0500-8

87. Miles C.J., Behr E.R. The role of genetic testing in unexplained sudden death // Transl Res. 2016. Vol. 168. P. 59–73. DOI: 10.1016/j.trsl.2015.06.007

88. Behr E., Wood D.A., Wright M., et al. Cardiological assessment of first-degree relatives in sudden arrhythmic death syndrome // Lancet. 2003. Vol. 362, No. 9394. P. 1457–1459. DOI: 10.1016/s0140-6736(03)14692-2

89. Behr E.R., Dalageorgou C., Christiansen M., et al. Sudden arrhythmic death syndrome: familial evaluation identifies inheritable heart disease in the majority of families // Eur Heart J. 2008. Vol. 29, No. 13. P. 1670–1680. DOI: 10.1093/eurheartj/ehn219

90. Kumar S., Peters S., Thompson T., et al. Familial cardiological and targeted genetic evaluation: low yield in sudden unexplained death and high yield in unexplained cardiac arrest syndromes // Heart Rhythm. 2013. Vol. 10, No. 11. P. 1653–1660. DOI: 10.1016/j.hrthm.2013.08.022

91. McGorrian C., Constant O., Harper N., et al. Family-based cardiac screening in relatives of victims of sudden arrhythmic death syndrome // Europace. 2013. Vol. 15, No. 7. P. 1050–1058. DOI: 10.1093/europace/eus408

92. Mellor G., Raju H., de Noronha S.V., et al. Clinical characteristics and circumstances of death in the sudden arrhythmic death syndrome // Circ Arrhythm Electrophysiol. 2014. Vol. 7, No. 6. P. 1078–1083. DOI: 10.1161/CIRCEP.114.001854

93. Papadakis M., Papatheodorou E., Mellor G., et al. The diagnostic yield of Brugada syndrome after sudden death with normal autopsy // J Am Coll Cardiol. 2018. Vol. 71, No. 11. P. 1204–1214. DOI: 10.1016/j.jacc.2018.01.031

94. Mellor G., Nelson C.P., Robb C., et al. The prevalence and significance of the early repolarization pattern in sudden arrhythmic death syndrome families // Circ Arrhythm Electrophysiol. 2016. Vol. 9, No. 6. ID e003960. DOI: 10.1161/CIRCEP.116.003960

95. Priori S.G., Wilde A.A., Horie M., et al. Executive summary: HRS/EHRA/APHRS expert consensus statement on the diagnosis and management of patients with inherited primary arrhythmia syndromes // Europace. 2013. Vol. 15, No. 10. P. 1389–1406. DOI: 10.1093/europace/eut272

96. van der Werf C., Stiekema L., Tan H.L., et al. Low rate of cardiac events in first-degree relatives of diagnosis-negative young sudden unexplained death syndrome victims during follow-up // Heart Rhythm. 2014. Vol. 11, No. 10. P. 1728–1732. DOI: 10.1016/j.hrthm.2014.05.028

97. Wong L.C.H., Roses-Noguer F., Till J.A., Behr E.R. Cardiac evaluation of pediatric relatives in sudden arrhythmic death syndrome: a 2-center experience // Circ Arrhythm Electrophysiol. 2014. Vol. 7, No. 5. P. 800–806. DOI: 10.1161/CIRCEP.114.001818

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Research article

Incidence of Coronary Embolism in Group of Patients with Atrial Fibrillation and Myocardial Infarction

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Embolic myocardial infarction (EMI) is more common than gets to be diagnosed. EMI is often associated with atrial fibrillation (AF). The incidence of this pathology, prognosis and treatment tactics remain unclear.

AIM: To assess the incidence of EMI among patients with myocardial infarction (MI), genesis of coronary embolism (CE), initial characteristics, treatment and prognosis in group of patients with EMI.

MATERIALS AND METHODS: The group of patients with EMI was selected among 1989 patients with MI admitted to the cardiology department of the North-Western State Medical University named after I.I. Mechnikov between 2013 to December 2019. The CE verification criteria were the SUITA criteria. Statistical data processing was carried out using the SAS program.

RESULTS: 16 cases of EMI were registered (0.8% of all MI and 4.3% of patients with MI and AF). 68.7% (95% CI = 41.5%–88.9%) of patients with EMI had AF. All patients with EMI and AF did not have adequate anticoagulant therapy before admission. Among patients with EMI, men predominated, they were younger, had fewer comorbidities than patients with MI and without AF. 13 of 16 patients with EMI were prescribed anticoagulants. During hospitalization, the composite endpoint (pulmonary embolism + stroke + cardiovascular death) was recorded in 25% (95% CI = 7.3%–52.2%), in the long-term period — in 30% of cases (95 % CI = 6.7–65.2). All these patients had AF. EMI in patients with AF was associated with the development of severe chronic heart failure (CHF) by the time of discharge and with decompensation of CHF in the long-term period.

CONCLUSIONS: EMI often occur in group of patients with AF, always in the absence of adequate anticoagulant therapy. Patients with EMI and AF have a worse prognosis due to recurrent thromboembolic events.

Keywords: anticoagulants; atrial fibrillation; coronary embolism; embolic myocardial infarction; prognosis; thrombaspiration.

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Научная статья

Встречаемость коронарной эмболии у пациентов с фибрилляцией предсердий, перенесших инфаркт миокарда

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Актуальность. Эмбологенный инфаркт миокарда (ЭИМ) встречается гораздо чаще, чем диагностируется. Наиболее распространенными признаны ЭИМ, ассоциированные с фибрилляцией предсердий (ФП). Однако реальная встречаемость данной патологии, прогноз, а также тактика лечения остаются до конца неясными.

Цель — оценить встречаемость ЭИМ среди больных с инфарктом миокарда (ИМ), генез коронарной эмболии (КЭ), исходные характеристики больных с ЭИМ, особенности лечения пациентов с ЭИМ, прогноз.

Материалы и методы. В период с 1 января 2013 по 31 декабря 2019 г. среди 1989 пациентов, поступивших в кардиологическое отделение СЗГМУ им. И.И. Мечникова с диагнозом ИМ, была отобрана группа больных с ЭИМ. Критериями верификации КЭ являлись критерии SUITA. Статистическая обработка данных проведена в программе SAS.

Результаты. Зарегистрировано 16 случаев ЭИМ (0,8% от числа всех ИМ и 4,3% от больных с ИМ и ФП). ЭИМ чаще развивался у пациентов с ФП — в 68,7% случаев (95% ДИ = 41,5%–88,9%). Все больные с ЭИМ и ФП до госпитализации не получали адекватной антикоагулянтной терапии. Среди пациентов с ЭИМ преобладали мужчины, они были моложе, имели меньше сопутствующих заболеваний по сравнению с больными с ИМ без ФП. 13 из 16 пациентов с ЭИМ были назначены антикоагулянты. В ходе госпитализации комбинированная конечная точка (тромбоэмболия легочной артерии + инсульт + сердечно-сосудистая смертность) была зарегистрирована у 25% больных (95% ДИ = 7,3%–52,2%), в отдаленном периоде — у 30% пациентов (95% ДИ = 6,7–65,2). Все эти больные имели ФП. ЭИМ у пациентов с ФП были ассоциированы с развитием тяжелой хронической сердечной недостаточности (ХСН) к моменту выписки, а также с декомпенсацией ХСН в отдаленном периоде.

Заключение. ЭИМ чаще развивается у пациентов с ФП, всегда при отсутствии адекватной антикоагулянтной терапии. Пациенты с ЭИМ и ФП имеют неблагоприятный прогноз, обусловленный рецидивирующими тромбоэмболическими событиями.

Ключевые слова: антикоагулянты; коронарная эмболия; прогноз; тромбаспирация; фибрилляция предсердий; эмбологенный инфаркт миокарда.

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LIST OF ABBREVIATIONS:

VKA — vitamin K antagonist
AC – anticoagulant
ATT — antithrombotic therapy
CI — confidence interval
MI — myocardial infarction
CA — coronary artery
CAG — coronary angiography
CEP — composite endpoint
CE — coronary embolism
OCT — optical coherence tomography
DOAC — direct oral anticoagulant
PE — pulmonary embolism
FC — functional class
AF — atrial fibrillation
CHF — chronic heart failure
PCI — percutaneous coronary intervention
EMI — embologenic myocardial infarction

INTRODUCTION

Embologenic myocardial infarction (EMI) is traditionally considered a rare pathology. According to the results of individual studies, EMI account for 0.8–13% of all cases of myocardial infarction (MI) [1–4]. However, the incidence of EMI in real clinical practice is currently unknown, due to the fact that there are few large studies on this topic [5]. In addition, scientists studying this problem agree that EMI happens more common than gets to be diagnosed [3, 4].

EMI is type 2 MI according to the Fourth Universal Definition [6]. It is caused by embolism in the coronary arteries (CA). The causes of coronary embolism (CE) can be in atrial fibrillation (AF), vegetations during infective endocarditis, valvular pathology (mitral and aortic stenosis, prosthetic heart valves), paradoxical embolism through an atrial septal defect due to venous thrombosis, tumors, dilated and hypertrophic cardiomyopathy, hypercoagulable conditions. Currently, AF-associated EMI are recognized as the most common [3, 4, 7].

Literature review shows that patients with EMI have an unfavorable long-term prognosis [2, 3, 8]. However, published studies have not compared prognosis for EMI with and without AF. Currently, there are also no clear recommendations on antithrombotic therapy (ATT) in patients with EMI, there are no unequivocal data on the appropriateness and optimal methods of percutaneous coronary intervention (PCI) in this group of patients.

AIM

To assess the incidence of EMI among patients with MI, as well as those with MI and AF according to the data of the cardiology department of a multi-specialty hospital, to establish the genesis of CE, the initial characteristics of EMI patients, the features of ATT and PCI in patients with EMI, hospital and long-term prognosis.

MATERIALS AND METHODS

Between January 1, 2013 and December 31, 2019 (2013-2019, inclusive), a group of patients with EMI was selected among all patients admitted to the cardiology department of the North-Western State Medical University named after I.I. Mechnikov of the Ministry of Health of Russia with MI diagnosis [9]. MI was diagnosed on the basis of the clinical picture, anamnesis, and laboratory and instrumental data according to Russian recommendations [10–12]. The CE verification criteria were the SUITA criteria [3]. Major criteria for CE include: angiographically proven CE without an atherosclerotic component, simultaneous embolism of several coronary arteries, concomitant systemic embolism without thrombosed left ventricular aneurysm. Minor criteria for CE are: a confirmed source of CE based on the results of transesophageal or transthoracic echocardiography, computed tomography or magnetic resonance imaging, the presence of risk factors for embolism, such as AF, a prosthetic valve, infective endocarditis, and others. CE is considered probable when 1 major criterion and 1 minor criterion are combined or 2 minor criteria are present; CE is proven when 2 major criteria, 1 major criterion and 2 minor, 3 minor criteria are combined. The diagnosis of EMI should be excluded in cases where atherosclerotic plaques are detected in the infarct-related coronary artery, narrowing the lumen of the vessel by more than 25%, unstable atherosclerotic plaques are observed, or ectasia of the coronary arteries occurs. [3].

All patients with EMI signed an informed consent before participation in the study. The study protocol was approved by the local ethics committee.

A standard examination of patients was performed according to Russian recommendations for the diagnosis and treatment of MI [10–12]. It included coronary angiography (CAG), and in controversial cases, optical coherence tomography (OCT).

After discharge from the hospital, patients visited the clinic once a year, whenever the visits were impossible, telephone surveys were carried out. Five patients didn't visit and refused to participate in the telephone surveys. The follow-up period for patients with EMI was 2.32(2.55) years, median (Me) = 2.06.

The study dealt with the incidence of EMI among patients with MI, as well as those with MI and AF, the initial characteristics of patients with EMI (gender, age, comorbid pathology), the composition of ATT, and the characteristics of PCI in this group of patients. In addition, the following in-hospital and long-term events in patients with EMI were assessed: relapse/re-MI, stroke, pulmonary embolism (PE), cardiovascular and overall mortality, composite endpoint (CEP) 1 (relapse/re-MI + stroke + cardiovascular mortality),

CEP 2 (PE + stroke + cardiovascular mortality)), functional class (FC) of chronic heart failure (CHF) at the time of discharge, hospitalization due to CHF decompensation after discharge, small and large bleeding. The TIMI group criteria were used to assess bleeding volume [13].

Statistical data processing was carried out using the SAS program (SAS Institutes Inc., USA). In a normal distribution, quantitative traits are described using the arithmetic mean and standard deviation (M(SD)); with an abnormal distribution — the arithmetic mean, standard deviation and median with an interquartile range (M(SD)/Me(IQR)). The prognosis, due to the descriptive nature of this work, is described with the number of events, the proportion of the event, and the 95% exact confidence interval (CI) of Clopper-Pearson, adjusted for the small sample size.

RESULTS

From January 1, 2013 to December 31, 2019 (2013-2019, inclusive) 1989 patients with MI were admitted to the department, of which 372 patients had AF. During the observation period, 16 cases of EMI were registered, which accounted for 0.8% of all patients with MI and 4.3% of patients with MI and AF. In accordance with the SUITA criteria [3], EMI diagnosis was proven in 8 cases and considered probable in the rest of the patients.

AF was registered in 11 out of 16 patients with EMI, which accounted for 68.7% of cases (95% CI = 41.5% – 88.9%). In 10 of 11 cases, there was a pre-existing AF. In 1 patient, the cause of EMI was hereditary thrombophilia, another 1 patient underwent EMI together with dilated cardiomyopathy with a pronounced effect of spontaneous contrast enhancement according to echocardiography. In 3 patients, the genesis of EMI was not detected.

Among patients with EMI, there were more men compared with patients with myocardial infarction and atrial fibrillation (10 of 16 patients — 62.5% (95% CI = 35.4% – 84.8%) vs. 47.6%, respectively. The mean age was 64.3 (15.1) years and 75.2 (10.1) years, respectively.

14 out of 16 patients with EMI had hypertension, 3 patients suffered from diabetes mellitus. In 3 of the 16 cases EMI patients had a history of a previous MI, and 6 had a stroke. Patients with EMI did not have severe dyslipidemia, were overweight (body mass index (M(SD)) = 26.0 (4.7) kg/m^2), had moderate decrease in renal function (glomerular filtration rate (M(SD)) = 60.0 (21.8) ml/min/1.73 m^2). All patients with EMI and AF had a high risk of thromboembolic complications according to the CHA2DS2-VASc scale (3.6(1.6) points) and did not take anticoagulants (ACs) before hospitalization due to MI or used them inadequately (incorrect doses or irregular intake).

Upon admission patients with EMI most often complained of intense pain in the chest (in 12 of 16 cases of EMI), less often of choking (4 cases), pain in the epigastric region (1 patient). Loss of consciousness was registered in 1 case. In 10 out of 16 cases of EMI, ST elevation MI occurred. Hemodynamically significant arrhythmias (sinoatrial and atrioventricular blockades, ventricular fibrillation) were not registered in patients with EMI. The mean ejection fraction (M(SD)/ Me(IQR)) was 50.4 (14.3)/53.5 (14.0)%.

According to CAG data, CAs were intact in 4 cases. These patients underwent an additional OCT, and signs of atherosclerotic lesions and coronary dissection were excluded. 10 patients had embolic occlusion of 1 CA; 2 patients had embolic occlusion of 2 CAs. Most often (in 6 cases), the infarct-related coronary artery was the circumflex artery, less often it was due to the right coronary artery (2 cases) and the anterior interventricular artery (2 cases). In 2 patients, CE was verified simultaneously in the circumflex artery and the anterior interventricular artery. Distal CE occurred in 6 cases. 1 patient had a proximal lesion of one CA and a distal lesion of the other. In the rest of the patients, CE was detected in the proximal parts of the arteries.

Considering intact CAs, as well as extremely distal CEs, revascularization was not recommended for 7 patients with EMI. Thrombolysis performed in only 1 case had no significant effect. Thrombaspiration was performed in 9 patients with EMI, that is, it was the most common tactic of PCI. In 5 cases it was combined with infarction-associated artery angioplasty, in 2 cases stenting was also applied.

During admission, 13 out of 16 patients with EMI took AC, of which 3 patients were prescribed triple ATT (acetylsalicylic acid + clopidogrel + AC), 8 patients received double ATT (clopidogrel + AC). The volume of ATT was determined depending on the ratio of ischemic and hemorrhagic risks. Triple ATT was prescribed for a period of 1 month, with a further transition to double ATT for up to 12 months; 1 year after the endured EMI, permanent intake of AC only was recommended. In 12 out of 13 cases, direct oral ACs (DOACs) were prescribed as ACs, and in 1 case it was a vitamin K antagonist (VKA). AC was not prescribed to 3 patients with a probable diagnosis of EMI and unknown etiology of CE. After 1 year, all patients who remained under observation (10 people) took AC, 3 of them — irregularly and / or in incorrect doses.

Noteworthy is the high incidence of both in-hospital (table 1) and out-of-hospital (table 2) thromboembolic events in patients with EMI. Moreover, during hospitalization, all of them were registered in patients on the first day of AF-associated EMI.

The only death during hospitalization was associated with massive PE.

By the time of discharge from the hospital, patients with EMI often developed severe CHF(FC III): in 5 out of 15 discharged patients. 7 patients had CHF II FC, 3 of them had I FC. It should be noted that all cases of severe CHF at discharge, and later episodes of decompensated CHF, occurred in patients with AF-associated EMI.

All events in the long-term period also had a thromboembolic origin and were registered in patients with

Table 1. In-hospital Events in Patients with embolic myocardial infarction

In-hospital event	EMI patients (*n* = 16), abs. (%)	%, 95% CI
MI recurrence	0 (0)	–
Cardioembolic stroke	2(12.5)	1.6–38.3
PE	3(18.7)	4.1–45.6
Major bleeding	1(6.25)	0.2–30.2
Minor bleeding	1(6.25)	0.2–30.2
Mortality	1(6.25)	0.2–30.2
CEP 1	3(18.7)	4.1–45.6
CEP 2	4(25.0)	7.3–52.2

Table 2. Long-term events in patients with embolic myocardial infarction

Long-term event	EMI patients (*n* = 10)*, abs. (%)	%, 95% CI
Reoccurring EMI	1(10.0)	0.2–44.5
Cardioembolic stroke	2(20.0)	2.5–55.6
PE	0(0)	–
Major bleeding	0(0)	–
Minor bleeding	2(20.0)	2.5–55.6
Mortality	2(20.0)	2.5–55.6
Admissions due to decompensation of CHF	4(40.0)	12.2–73.7
CEP 1	3(30.0)	6.7–65.2
CEP 2	3(30.0)	6.7–65.2

Note: * Patients who died during admission, as well as those who dropped out of the study after admission, were excluded from the study.

AF-associated EMI 1.9–6.9 years after admission.All cases were happening while withdrawal or inadequate intake of AC. In the long term, 2 patients died. The cause of death in 1 case was cardioembolic stroke. The mechanism of death of the second patient could not be reliably deduced. Both patients, who died in the long-term period, suffered massive PE simultaneously with EMI during admission.

In patients with EMI, the number of bleedings both during admission (table 1) and in the long-term period (table 2) was small. There were only 4 episodes during the entire follow-up period, of which only 1 major bleeding was associated with PCI during hospitalization (post-puncture hematoma of the thigh) in a patient taking multicomponent ATT. The remaining bleedings were minor, occurred in presence of taking AC and were registered in patients with predisposing factors (microhematuria associated with exacerbation of chronic pyelonephritis, gingival bleeding in a patient with periodontal disease, minor gastrointestinal bleeding associated with erosive gastritis).

DISCUSSION

Previously, it was believed that CE was impossible for a number of reasons: coronary filling occurs in diastole, the presence of differences between the diameters of the aorta and the CA, the deviation of the CA from the aortic root at a right angle, high volume and velocity blood flows in this part of the aorta [4, 7]. However, in 1978, K.R. Prizel et al., in a post-mortem study of 419 cases of MI, showed that CE occurred in 13.0% of them. Moreover, AF occurred in 24.0% of patients with CE [4]. The work of K.R. Prizel with co-authors gave the foundation for further research into the EMI problem.

EMI occur in real clinical practice. According to the literature, this type of MI is considered a rather rare pathology [1–4]. This may be due not only to their low prevalence, but also to the following difficulties that arise when verifying the diagnosis of EMI: the absence of clinical features compared to the “classic” case of MI, the need to identify the source of CE, and also exclusions of atherosclerotic plaque rupture in an infarction-related KA.

In the present study, EMI was 0.8% of all MIs. The diagnosis was verified using the SUITA criteria [3], which were also used in most of the large works devoted to the problem of EMI [1, 2, 8]. In doubtful cases due to the absence of typical angiographic signs, OCT was performed to rule out an atherosclerotic lesion in the infarct-related coronary artery and to confirm the embolic nature of MI.

In the present study, in most cases (68.7%), EMI was associated with AF, which corresponds to the literature data [3, 4, 7]. Moreover, EMI developed in those AF patients who had high risks of thromboembolic complications according to the CHA2DS2-VASc scale and did not take adequate anticoagulants. As in most large studies [2–4], in our study, patients with EMI were dominated by men, they were younger, and had fewer comorbidities compared with patients with type 1 MI.

As previously mentioned, there are currently no guidelines for the treatment of patients with EMI. The existing literature suggests, there are only data from individual authors, according to which thromboaspiration is the preferred method of PCI in patients with EMI [2, 3, 8]. In the present study, thromboaspiration was most often performed in combination with angioplasty; rarely, if this tactic was not effective enough, stenting was performed. In all cases, a satisfactory angiographic result was obtained. In a number of patients with EMI, given the angiographic picture, there was no need for revascularization.

The question of the volume of ATT during EMI remains open. Some experts believe that it is necessary to take AC with one antiplatelet agent, while others believe that only AC is sufficient [1, 14, 15]. In the case of coronary artery stenting in AF-associated EMI, recommendations for patients with AF who have undergone MI and PCI should be followed. In the present study, when prescribing ATT, the current recommendations for the treatment of patients with acute coronary syndrome and recommendations for the treatment of patients with AF [16–18] were used. Most of our patients had clear indications for the AC administration (AF, thrombophilia, the effect of spontaneous contrast enhancement). Despite the multicomponent nature of ATT (antiplatelet agents + AC) in most of the patients in the study, the number of bleedings was small. An unfavorable prognosis was associated only with a violation of the prescribed ATT regimens, namely with inadequate intake or withdrawal of AC.

In this study, in 25.0% of patients with EMI during admission, CEP (PE + stroke + cardiovascular mortality) was registered, which echoes the results of the SUITA study, in which concomitant EMI systemic embolism occurred in 23.0% of patients [3]. In most studies, EMI was associated with poor long-term prognosis after hospital discharge due to repeated EMI and strokes [2, 3, 8]. In the present work, the majority of thromboembolic events, all deaths, both during admission and in the long-term period, occurred in patients with AF-associated EMI. In the long-term period, those patients died in whom CE was initially combined with systemic embolism of other localizations, as well as after repeated thromboembolic episodes, and always in the presence of withdrawal or inadequate intake of AC.

CONCLUSION

Patients with EMI and AF are at the highest risk because of poor long-term prognosis due to recurrent thromboembolic events.

At the moment, there are still questions related to the treatment of patients with EMI: the feasibility and methods of PCI, the amount of ATT, which require further study in order to optimize the tactics of treating such patients.

Due to constant increase in the number of patients with AF, an increase in the prevalence of EMI should be expected. In this regard, it is necessary to remember about this diagnosis, apply the SUITA criteria, perform CAG and (in controversial cases) OCT in order to keep this pathology in focus.

ADDITIONAL INFORMATION

Conflict of interests. All authors declare no conflicts of interest.

REFERENCES

1. Frolov AA, Sharabrin EG, Savenkov AG, Botova SN. Embologenic myocardial infarction: the view of endovascular surgeon. *Cardiology. News, Opinions, Training*. 2016;(2):54–58. (In Russ.).

2. Popovic B, Agrinier N, Bouchahda N, et al. Coronary embolism among ST-segment–elevation myocardial infarction patients. Mechanisms and management. *Circulation. Cardiovascular interventions*. 2018;11(1):e005587. DOI: 10.1161/CIRCINTERVENTIONS.117.005587

3. Shibata T, Kawakami S, Noguchi T, et al. Prevalence, clinical features, and prognosis of acute myocardial infarction attributable to coronary artery embolism. *Circulation*. 2015;132(4):241–250. DOI: 10.1161/CIRCULATIONAHA.114.015134

4. Prizel KR, Hutchins GM, Bulkley BH. Coronary artery embolism and myocardial infarction. A clinicopathologic study of 55 patients. *Ann Intern Med.* 1978;88(2):155–161. DOI: 10.7326/0003-4819-88-2-155

5. Boldueva SA, Soloveva MV, Oblavatckii DV, Feoktistova VS. Myocardial Infarction in the Group of Patients With Atrial Fibrillation. *Kardiologiia*. 2020;60(1):53–61. (In Russ.). DOI: 10.18087/cardio.2020.1.n620

6. Thygesen K, Alpert JS, Jaffe AS, et al. Fourth universal definition of myocardial infarction 2018. *Eur Heart J*. 2018;40(3):237–269. DOI: 10.1093/eurheartj/ehy462
7. Manchurov VN, Anisimov KV, Oskanov MB, et al. Myocardial infarction due to coronary artery embolism. *Kardiologiia*. 2018;58(2):83–90. (In Russ.). DOI: 10.18087/cardio.2018.2.10090
8. Huang AL, Murphy JC, Shaw E, et al. Routine aspiration thrombectomy improves the diagnosis and management of embolic myocardial infarction. *Catheter Cardiovasc Interv*. 2016;87(4): 642–647. DOI: 10.1002/ccd.26047
9. Solov'eva MV. *Osobennosti techeniya i prognoz infarkta miokarda u bol'nykh s fibrillyatsiei predserdii* [dissertation abstract]. Saint Petersburg, 2022. 24 p. (In Russ.).
10. Ruda MYa, Averkov OV, Golitsyn SP, et al. Diagnosis and management of ST-segment elevation myocardial infarction. *Russian cardiology bulletin*. 2014;9(4):3–60. (In Russ.).
11. Ruda MY, Averkov OV, Panchenko EP, Yavelov IS. Recommendations of the Society of Specialists in Urgent Cardiology. Diagnosis and Treatment of Patients With Non-ST-Segment Elevation Acute Coronary Syndrome. Part 1. *Kardiologiia*. 2017;57(8):80–100. (In Russ.). DOI: 10087/cardio.2017.8.10023
12. Ruda MY, Averkov OV, Panchenko EP, Yavelov IS. Recommendations of the Society of Specialists in Urgent Cardiology Diagnosis and Treatment of Patients With Non-ST-Segment Elevation Acute Coronary Syndrome. Part 2. *Kardiologiia*. 2017;57(9):83–96. (In Russ.). DOI: 10087/cardio.2017.9.10026
13. Rao AK, Pratt C, Berke A, et al. Thrombolysys in Myocardial Infarction (TIMI) Trial-phase I: hemorragic manifestations and changes in plasma fibrinogen and the fibrinolytic system in patients treated with recombinant tissue plasminogen activator and streptokinase. *J Am Coll Cardiol*. 1988;11(1):1–11. DOI: 10.1016/0735-1097(88)90158-1
14. Jiao Z-Y, Zhang D-P, Xia K, et al. Clinical analysis of acute myocardial infarction caused by coronary embolism. *J Thorac Dis*. 2017;9(9):2898–2903. DOI: 10.21037/jtd.2017.07.92
15. Kolodgie FD, Virmani R, Finn AV, Romero ME. Embolic myocardial infarction as a consequence of atrial fibrillation a prevailing disease of the future. *Circulation*. 2015;132(4):223–226. DOI: 10.1161/CIRCULATIONAHA.115.017534
16. Roffi M, Patrono C, Collet J-P, et al. 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. *Eur Heart J*. 2016;37(3):267–315. DOI: 10.1093/eurheartj/ehv320
17. Kirchhof P, Benussi S, Kotecha D, et al. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. *Eur Heart J*. 2016;37(38):2893–2962. DOI: 10.1093/eurheartj/ehw210
18. Ibanez B, James S, Agewall S, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. *Eur Heart J*. 2018;39(2):119–177. DOI: 10.1093/eurheartj/ehx393

СПИСОК ЛИТЕРАТУРЫ

1. Фролов А.А., Шарабрин Е.Г., Савенков А.Г., Ботова С.Н. Эмбологенный инфаркт миокарда: взгляд эндоваскулярного хирурга // Кардиология: новости, мнения, обучение. 2016. № 2. С. 54–58.
2. Popovic B., Agrinier N., Bouchahda N., et al. Coronary embolism among ST-segment–elevation myocardial infarction patients. Mechanisms and management // Circulation. Cardiovascular interventions. 2018. Vol. 11, No. 1. ID e005587. DOI: 10.1161/CIRCINTERVENTIONS.117.005587
3. Shibata T., Kawakami S., Noguchi T., et al. Prevalence, clinical features, and prognosis of acute myocardial infarction attributable to coronary artery embolism // Circulation. 2015. Vol. 132, No. 4. P. 241–250. DOI: 10.1161/CIRCULATIONAHA.114.015134
4. Prizel K.R., Hutchins G.M., Bulkley B.H. Coronary artery embolism and myocardial infarction. A clinicopathologic study of 55 patients // ***Ann Intern Med***. 1978. Vol. 88, No. 2. P. 155–161. DOI: 10.7326/0003-4819-88-2-155
5. Болдуева С.А., Соловьева М.В., Облавацкий Д.В., Феоктистова В.С. Инфаркт миокарда у больных с фибрилляцией предсердий // Кардиология. 2020. Т. 60, № 1. С. 53–61. DOI: 10.18087/cardio.2020.1.n620
6. Thygesen K., Alpert J.S., Jaffe A.S., et al. Fourth universal definition of myocardial infarction 2018 // Eur Heart J. 2018. Vol. 40, No. 3. P. 237–269. DOI: 10.1093/ eurheartj/ehy462
7. Манчуров В.Н., Анисимов К.В., Осканов М.Б., и др. Инфаркт миокарда эмболической природы // Кардиология. 2018. Т. 58, № 2. С. 83–90. DOI: 10.18087/cardio.2018.2.10090
8. Huang A.L., Murphy J.C., Shaw E., et al. Routine aspiration thrombectomy improves the diagnosis and management of embolic myocardial infarction // Catheter Cardiovasc Interv. 2016. Vol. 87, No. 4. P. 642–647. DOI: 10.1002/ccd.26047
9. Соловьева М.В. Особенности течения и прогноз инфаркта миокарда у больных с фибрилляцией предсердий: автореф. дис. ... канд. мед. наук. Санкт-Петербург, 2022. 24 с.
10. Руда М.Я., Аверков О.В., Голицын С.П., и др. Диагностика и лечение больных острым инфарктом миокарда с подъемом сегмента ST электрокардиограммы: Клинические рекомендации // Кардиологический вестник. 2014. Т. 9, № 4. С. 3–60.
11. Руда М.Я., Аверков О.В., Панченко Е.П., Явелов И.С. Диагностика и лечение больных с острым коронарным синдромом без подъема сегмента ST электрокардиограммы: Рекомендации Общества специалистов по неотложной кардиологии. Часть 1 // Кардиология. 2017. Т. 57, № 8. С. 80–100. DOI: 10087/cardio.2017.8.10023
12. Руда М.Я., Аверков О.В., Панченко Е.П., Явелов И.С. Диагностика и лечение больных с острым коронарным синдромом без подъема сегмента ST электрокардиограммы: Рекомендации Общества специалистов по неотложной кардиологии. Часть 2 // Кардиология. 2017. Т. 57, № 9. С. 83–96. DOI: 10087/cardio.2017.9.10026
13. Rao A.K., Pratt C., Berke A., et al. Thrombolysys in Myocardial Infarction (TIMI) Trial-phase I: hemorragic manifestations and changes in plasma fibrinogen and the fibrinolytic system in

patients treated with recombinant tissue plasminogen activator and streptokinase // J Am Coll Cardiol. 1988. Vol. 11, No. 1. P. 1–11. DOI: 10.1016/0735-1097(88)90158-1

14. Jiao Z.-Y., Zhang D.-P., Xia K., et al. Clinical analysis of acute myocardial infarction caused by coronary embolism // J Thorac Dis. 2017. Vol. 9, No. 9. P. 2898–2903. DOI: 10.21037/jtd.2017.07.92

15. Kolodgie F.D., Virmani R., Finn A.V., Romero M.E. Embolic myocardial infarction as a consequence of atrial fibrillation a prevailing disease of the future // Circulation. 2015. Vol. 132, No. 4. P. 223–226. DOI: 10.1161/CIRCULATIONAHA.115.017534

16. Roffi M., Patrono C., Collet J.-P., et al. 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation // Eur Heart J. 2016. Vol. 37, No. 3. P. 267–315. DOI: 10.1093/eurheartj/ehv320

17. Kirchhof P., Benussi S., Kotecha D., et al. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS // Eur Heart J. 2016. Vol. 37, No. 38. P. 2893–2962. DOI: 10.1093/eurheartj/ehw210

18. Ibanez B., James S., Agewall S., et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation // Eur Heart J. 2018. Vol. 39, No. 2. P. 119–177. DOI: 10.1093/eurheartj/ehx393

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Research article

Factors Associated with a Positive Hemodynamic Response to Cardiac Resynchronization Therapy

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AIM: This study aimed to conduct a comparative analysis of clinical, electrocardiographic, and echocardiographic factors in patients with chronic heart failure (CHF) with different hemodynamic responses to cardiac resynchronization (CRT) to assess the possibility of their use in predicting the positive effect of CRT.

MATERIALS AND METHODS: The study included 136 patients with New York Heart Association grade 3–4 CHF with a left ventricular ejection fraction of ⩽ 35%, QRS duration of ⩾ 150 ms, QRS duration of 130–149 ms, and QRS morphology of left bundle branch block (LBBB). For CHF treatment and primary prevention of sudden cardiac death, a cardioverter-defibrillator with CRT (CRT-D) function was implanted. The enrolled patients were followed up prospectively for 1 year to record the endpoint, namely, hemodynamic response to CRT, assessed by a decrease in the end-systolic volume of the left ventricle by ⩾ 15%.

RESULTS: During the 1-year follow-up, the primary endpoint was registered in 62 (46%) patients. With a one-way logistic regression, four indicators with the highest predictive potential ($p < 0.05$) and associated with the occurrence of the studied endpoint were identified. Based on the results of the multivariate regression analysis, a prognostic model was developed, which included three factors with the highest levels of statistical significance, namely, a history of indications of a previous correction of valvular insufficiency, QRS duration, and LBBB criteria according to Strauss. The diagnostic efficiency of the model was 73% (sensitivity, 80%; specificity, 68%). The electrocardiographic parameters of the Strauss LBBB criteria and QRS duration were independent predictors of the studied endpoint.

CONCLUSIONS: The developed multivariate prognostic model may be useful in the selection of patients with CHF reduced ejection fraction for implantation of devices with CRT function; the lack of external validation limits its application in practice.

Keywords: chronic heart failure; cardiac resynchronization therapy; response predictors; prognostic system.

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Оригинальные исследования

Факторы, ассоциированные с положительным гемодинамическим ответом на сердечную ресинхронизирующую терапию

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Цель исследования — провести сравнительный анализ клинических, электрокардиографических и эхокардиографических факторов у больных хронической сердечной недостаточностью (ХСН) с разным гемодинамическим ответом на проводимую сердечную ресинхронизирующую терапию (СРТ), оценить возможности их использования при прогнозировании положительного эффекта СРТ.

Материалы и методы. В исследование были включены 136 больных ХСН NYHA 3–4 функционального класса с фракцией выброса левого желудочка ⩽ 35% и длительностью QRS ⩾ 150 мс либо продолжительностью QRS 130–149 мс и морфологией QRS по типу блокады левой ножки пучка Гиса (БЛНПГ), которым для лечения ХСН и с целью первичной профилактики внезапной сердечной смерти была проведена имплантация кардиовертера-дефибриллятора с функцией сердечной ресинхронизирующей терапии (СРТ-Д). Включенные в исследование пациенты проспективно наблюдались в течение года для регистрации конечной точки — гемодинамического ответа на СРТ, оцененного по снижению конечного систолического объема левого желудочка на ⩾ 15%.

Результаты. В ходе 1-летнего наблюдения первичная конечная точка была зарегистрирована у 62 больных (46%). При однофакторной логистической регрессии выделено 4 исследуемых показателя с наибольшим прогностическим потенциалом ($p < 0,05$), связанных с возникновением исследуемой конечной точки. По результатам многофакторного регрессионного анализа была разработана прогностическая модель, в состав которой вошло три фактора, имеющих максимальные уровни статистической значимости: наличие в анамнезе указаний на ранее проведенную коррекцию клапанной недостаточности, продолжительность QRS, критерии БЛНПГ по Strauss. Диагностическая эффективность модели составила 73% (чувствительность 80%, специфичность 68%). Было обнаружено, что электрокардиографические показатели: критерии БЛНПГ по Strauss и продолжительность QRS — являются независимыми предикторами наступления изучаемой конечной точки.

Заключение. Разработанная многофакторная прогностическая модель может оказаться полезной в отборе больных ХСН с низкой фракцией выброса на имплантацию устройств с функцией СРТ, отсутствие внешней валидации ограничивает ее применение в практике.

Ключевые слова: хроническая сердечная недостаточность; сердечная ресинхронизирующая терапия; предикторы ответа; прогностическая система.

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INTRODUCTION

According to the Epidemiological Survey of Patients with CHF in Real Practice (EPOHA CHF study), the prevalence of chronic heart failure (CHF) in the Russian Federation has increased from 6.1% to 8.2% over the past 20 years [1], which explains the relevance of studying this medical problem.

The identification of disorders of interventricular and intraventricular conduction in patients with CHF led to the concept of cardiac resynchronization therapy (CRT) [2], which effectively eliminates electrical and mechanical dyssynchrony, improves the contractile function of the heart, and initiates reverse remodeling of the left ventricle [3]. Several studies have demonstrated that a decrease in left ventricular (LV) end-systolic volume (ESV) by ⩾ 15% is associated with a decrease in cardiovascular mortality in patients with CHF with reduced LV ejection fraction (CHF rEF) and therefore can be used as a reliable criterion for a positive hemodynamic response to CRT [4].

One of the most important and urgent problems in the use of CRT is insufficient response, which some researchers attribute to the inappropriate selection of patients for CRT. According to current recommendations, implantation of a CRT device is indicated for patients with CHF LVEF of ⩽ 35%, QRS duration of ⩾ 150 ms, or QRS duration of 130–149 ms and QRS morphology similar to left bundle branch block (LBBB) [5, 6]. This approach did not increase the number of patients who "responded" to CRT, which requires continued research in this field.

The work aimed to conduct a comparative analysis of clinical, electrocardiographic, and echocardiographic factors in patients with CHF with different hemodynamic responses to CRT and assess the possibility of their use in predicting the positive CRT effect.

MATERIALS AND METHODS

The presented material is a part of an ongoing single-center prospective clinical study conducted in accordance with the standards of Good Clinical Practice and the principles of the Declaration of Helsinki. The study protocol was approved by the local ethics committee of the Astrakhan State Medical University of the Ministry of Health of Russia (Minutes No. 3 of the LEC meeting dated 12/30/2021) and presented in the public register clinicaltrials.gov (NCT05539898). All patients under follow-up signed an informed consent to participate in the study.

Patient selection

The inclusion criteria were current indications for implantation of a biventricular implantable cardioverter-defibrillator (ICD) with CRT function (CRT-D) [5] and no history of sustained episodes of ventricular arrhythmias/sudden cardiac death. Exclusion criteria were as follows: hypertrophic cardiomyopathy, arrhythmogenic right ventricular dysplasia, verified hereditary channelopathies, and presence of indications for cardiac surgery (revascularization and correction of valvular insufficiency).

After testing for the inclusion/exclusion criteria, 180 patients who underwent CRT-D implantation were included in the study (Fig. 1). Device implantation was performed according to accepted methods [10]. A bipolar or

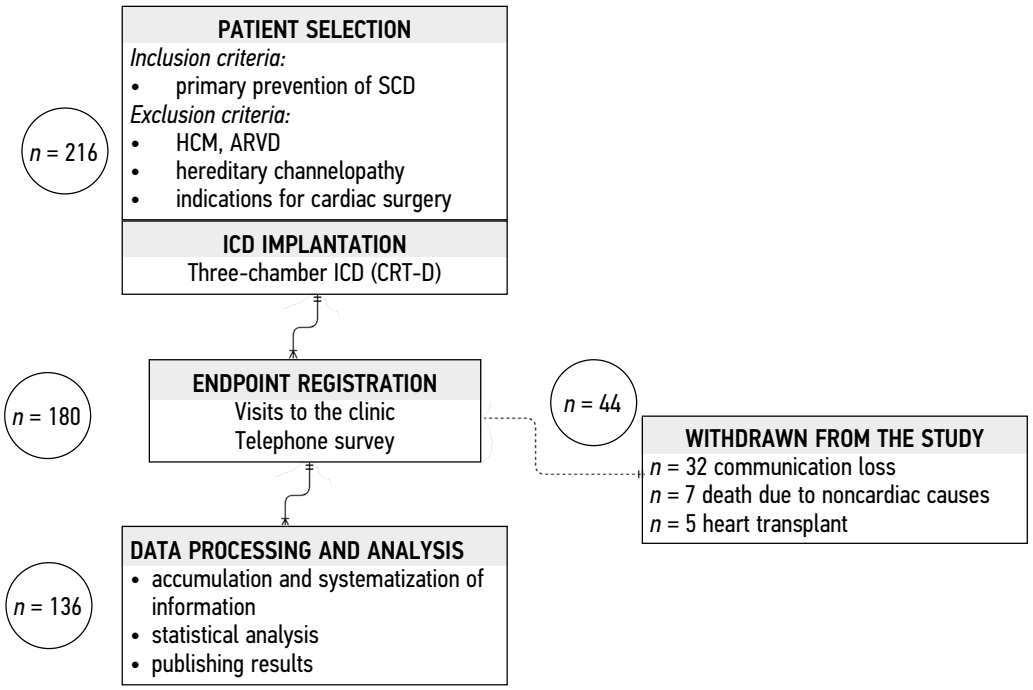

Fig. 1. Flow chart of the study design.

Note: ARVD, arrhythmogenic right ventricular dysplasia; CRT-D, implantable cardioverter defibrillator with cardiac resynchronization therapy function; HCM, hypertrophic cardiomyopathy; ICD, implantable cardioverter defibrillator; SCD, sudden cardiac death.

quadripolar LV lead was implanted using a delivery system into one of the coronary sinus veins. The lateral cardiac vein, which is usually located over the zone of late LV activation in patients with LBBB, was preferred for implantation.

To provide LV stimulation, a vector with a lower stimulation threshold and without stimulation of the phrenic nerve was chosen. Atrioventricular delay was performed to provide the maximum (approximately 100%) percentage of biventricular stimulation. Interventricular delay was determined by the minimum duration of the paced ventricular complex on the electrocardiogram (ECG). If delays can be selected, automatic algorithms of manufacturers were used [11]. ICD electrotherapy programming, protocol for recording and analyzing the ECG, and results of transthoracic echocardiography were described in detail previously [12, 13]. The presence of LBBB was determined according to the Strauss criteria [14].

Postoperative follow-up

Postoperative follow-up was performed for 12 months. The patients were invited to visit the clinic 3, 6, and 12 months after implantation. At this time, they were examined by a cardiologist, transthoracic echocardiography was performed, and if necessary, the programmed device parameters were corrected. In the case of cardiac decompensation, the patient can contact the investigator out of the schedule, the therapy was adjusted, and the clinical status was assessed jointly with cardiologists at the primary healthcare facility. Additionally, information about the occurrence of endpoints was obtained from the medical records, interviews of relatives, and messages analyzed from remote ICD monitoring (Medtronic Carelink, Biotronik HomeMonitoring).

The study endpoint was a hemodynamic response to CRT that was assessed by a decrease in LV ESV of ⩾ 15%.

Statistical analysis

Research data processed statistically using parametric and non-parametric analysis. Accumulation, adjustment, systematization of initial information, and visualization of the results were performed in Microsoft Office Excel 2010 spreadsheets. Statistical analysis was performed using IBM SPSS Statistics for Windows version 23 (IBM Corp., Armonk, NY, USA). Quantitative indicators were described and compared taking into account the distribution; those with normal distribution were assessed using the Kolmogorov–Smirnov test. When confirming the normality of the distribution, data were described using the arithmetic mean (*M*) and standard deviation. The comparison was performed using Student's *t*-test. In the absence of normal distribution, median (Me) and lower and upper quartiles (Q1–Q3) were indicated and were compared using the Mann–Whitney test. Nominal indicators were compared using Pearson's χ^2 test. When comparing relative indicators, the odds ratio (OR) was used as a quantitative measure of the effect. Significance was proven if the confidence interval (CI) was outside the border of no effect, which was taken as 1. The critical level of significance when testing statistical hypotheses was equal to 0.05. The multivariate prognostic model for determining the response to resynchronization therapy based on the studied ECG parameters was constructed using the binary logistic regression method. Independent variables were selected using the stepwise inverse selection method employing Waldovsky statistics as an exclusion criterion. The statistical significance of the resulting model was determined using Pearson's χ^2 test.

Nigelkirk's R2 was used as a measure of certainty, indicating the segment of the variance that can be explained by logistic regression. To assess the predictive value of the model and determine the threshold value of the resulting function at the cutoff point, receiver operating characteristics (ROC) analysis was performed with the calculation of the area under the curve.

RESULTS

A total of 136 patients completed the study protocol. The study endpoint was reported in 62(46%) patients. When analyzing the studied clinical and demographic indicators, the QRS duration, frequency of registration of Strauss LBBB, a history of previously performed surgical correction of valvular insufficiency, and permanent atrial fibrillation showed significant differences (Table 1).

These four factors were subjected to univariate and multivariate analyses (Table 2).

Using the binary logistic regression method, prognostic models were developed to determine the probability of hemodynamic response to CRT in patients with CHF rEF, based on the studied parameters.

The best predictive model was described by the following equation (1):

$$p = 1/(1+e^{-z})*100\ \%$$

$$z = -6.018 - 1.909*X_{valves} + 1.931*X_{LBBB} + 0.026*X_{QRS} \quad (1)$$

where p is the probability of cardiovascular death; X_{valves} — a history of correction of valvular insufficiency; X_{LBBB} — presence of LBBB according to Strauss; and X_{QRS} — duration of the QRS complex.

The resulting regression model was statistically significant (p = 0.001). Based on the value of Nigelkirk's determination coefficient, the model (1) takes into account 28.4% of the factors that determine the probability of a positive hemodynamic response to CRT.

The area under the ROC curve, which corresponds to the relationship between the prediction of the primary endpoint occurrence and the regression function value, was 0.768 ± 0.059 with 95% CI of 0.653–0.883 (Fig. 2).

The threshold value of function (1) at the cutoff point was 0.5. Values equal to or greater than this value corresponded to a good prognosis of a positive hemodynamic

Table 1. Comparative clinical and demographic characteristics of patients, depending on the endpoint achievement

Clinical indicator	All patients (*n* = 136)	Patients responding to CRT (*n* = 62)	Patients not responding to CRT (*n* = 74)	*P* 3–4
Age, years	56 (52–62)	56 (53–66)	55 (52–60)	0.844
Male sex, *n* (%)	108 (79)	46 (74)	62 (84)	0.250
BMI, kg/m^2	29.1 (25.7–31.8)	28.2 (25.6–32)	29 (26.6–32.1)	0.571
CHD, *n* (%)	42 (31)	16 (26)	26 (35)	0.287
PICS among patients with CHD, *n* (%)	24 (18)	8 (13)	16 (22)	0.270
DCM, *n* (%)	94 (69)	46 (74)	48 (65)	0.912
CHF grade 3, *n* (%)	119 (88)	56 (90)	63 (85)	0.221
CHF grade 4, *n* (%)	17 (13)	6 (10)	11 (15)	0.317
History of AH, *n* (%)	68 (50)	28 (45)	40 (54)	0.465
Diabetes mellitus, *n* (%)	28 (21)	8 (13)	20 (27)	0.128
Obesity, *n* (%)	54 (40)	24 (39)	30 (41)	0.878
Cerebral stroke, *n* (%)	10 (7)	2 (3)	8 (11)	0.238
CKD, *n* (%)	65 (48)	25 (41)	40 (54)	0.304
Anemia, *n* (%)	10 (7)	26 (10)	4 (6)	0.426
AF (paroxysmal/persistent), *n* (%)	32 (24)	20 (32)	12 (16)	0.103
AF (permanent form), *n* (%)	10 (7)	0	10 (14)	0.042
VTunst, *n* (%)	6 (4)	2 (3)	4 (5)	0.567
SBP, mm Hg	120 (110–130)	120 (110–135)	120 (110–135)	0.866
DBP, mm Hg	80 (70–80)	80 (70–80)	80 (70–80)	0.995
HR, bpm	75 (68–85)	76 (71–82)	75 (64–87)	0.445
PQ duration, ms	190 (160–200)	180 (160–190)	180 (160–200)	0.615
QRS duration, ms	170 (160–190)	180 (160–190)	160 (150–185)	0.035
Strauss LBBB, *n* (%)	110 (81)	58 (94)	52 (70)	0.015
LV end-systolic volume (mL/m^2)	95 (73–115)	95 (74–118)	82 (71–103)	0.182
LV end-diastolic volume (mL/m^2)	129 (102–156)	127 (110–154)	122 (100–135)	0.108
Simpson LV EF, %	29 (25–33)	29 (26–34)	30 (26–34)	0.710
LV relative wall thickness (cm)	0.31 (0.26–0.36)	0.30 (0.27–0.36)	0.32 (0.27–0.39)	0.348
LV mass index (g/m^2)	167 (137–205)	167 (136–185)	182 (133–221)	0.954
VLA (mL)	92 (76–120)	89 (84–93)	100 (79–104)	0.488
Pulmonary artery systolic pressure (mm Hg)	44 (31–56)	41 (30–53)	40 (31–55)	0.265
RVbas, cm	3.9 (3.4–4.5)	3.6 (3.5–3.6)	3.9 (3.5–4.6)	0.792
RVav, cm	3.3 (2.7–4.0)	2.5 (2.3–2.6)	3.0 (2.8–3.3)	0.410
TAPSE, cm	1.7 (0.8–1.9)	1.8 (1.7–1.8)	1.7 (1.2–1.95)	0.915
Surgical interventions on the heart:				
Revascularization (coronary bypass or percutaneous coronary intervention), *n* (%)	36 (26)	14 (23)	22 (30)	0.350
Valve insufficiency correction, n (%)	22 (16)	4 (6)	18 (24)	0.045
LV plastic surgery, *n* (%)	16 (12)	5 (8)	11 (15)	0.392
Quadripolar LV lead, *n* (%)	24 (16)	12 (19)	10 (14)	0.372
Received drug therapy:				
β-blockers, *n* (%)	136 (100)	62 (100)	74 (100)	0.913
ACE inhibitor/ARA II, *n* (%)	93 (68)	43 (69)	50 (67)	0.851
ARNI, *n* (%)	43 (32)	19 (31)	24 (33)	0.831
Mineralocorticoid antagonists, *n* (%)	121 (89)	54 (88)	67 (90)	0.154
Loop diuretics, *n* (%)	131 (96)	59 (95)	72 (97)	0.912
iSGCT-2, *n* (%)	11 (8)	5 (8)	6 (8)	0.381
Sotalol, *n* (%)	22 (16)	7 (11)	15 (20)	0.191
Amiodarone, *n* (%)	43 (32)	22 (35)	21 (29)	0.152

Note: Data are presented as absolute number of patients (%) or as *Me*(Q1–Q3) unless otherwise indicated. ACE inhibitors, angiotensin-converting enzyme inhibitors; AF — atrial fibrillation; AH, arterial hypertension; ARA II, angiotensin II receptor antagonists; ARNI, angiotensin receptors and neprilysin inhibitors; BMI, body mass index; CHD, coronary heart disease; CKD, chronic kidney disease; DBP, diastolic blood pressure; DCM, dilated cardiomyopathy; HR, heart rate; iSGCT-2, sodium-glucose cotransporter type 2 inhibitors; LVEF, left ventricular ejection fraction; PICS, postinfarction cardiosclerosis; SBP, systolic blood pressure; VTunst, unstable runs of ventricular tachyarrhythmias

Table 2. Relationship between the study factors and the primary endpoint

Factors	Univariate analysis			Multivariate analysis		
	OR	95% CI	*P*	OR	95% CI	*p*
AF (permanent form)	0.005	0.002–1.032	0.467	–	–	–
LBBB	6.135	1.242–30.292	0.026	6.896	1.310–36.307	0.023
QRS duration	1.026	1.002–1.050	0.034	1.026	1.000–1.053	0.048
Correction of valvular insufficiency in history	0.215	0.043–1.082	0.062	0.148	0.026–0.834	0.030

Note: AF, atrial fibrillation; CI, confidence interval; LBBB, complete blockade of the left bundle branch block; OR, odds ratio

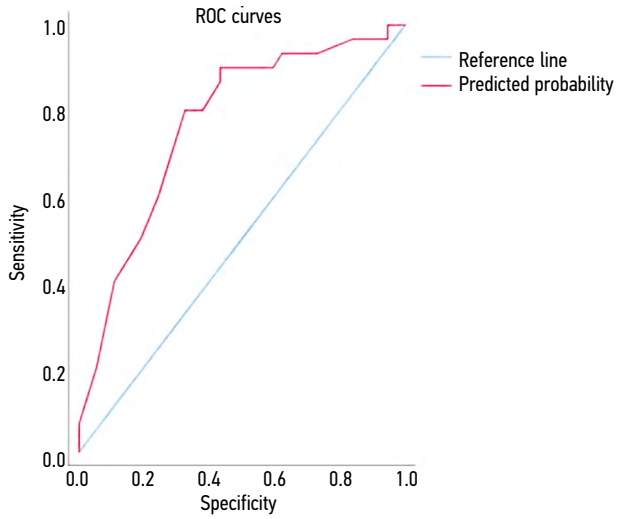

Fig. 2. ROC curve indicating the relationship between the probability of a hemodynamic response to CRT and the value of the regression equation obtained.

response to CRT. The sensitivity and specificity of the method were 80% and 68%, respectively.

DISCUSSION

Our results are consistent with the rate of positive hemodynamic response to CRT described in the literature. In previous major international multicenter studies involving a similar cohort of patients, this indicator (estimated as a decrease in LV ESV of ⩾15%) varied from 40% [15] to 56% [16].

In the course of achieving this aim, a model with a high prognostic metric (diagnostic efficiency of 73%) was proposed, which included one clinical and anamnestic factor and two electrocardiographic parameters.

The identification of the predictive potential of a history of indications of a previous correction of valvular insufficiency was quite unexpected. The authors who evaluated this factor revealed that it did not affect the efficiency of CRT [17]. Meanwhile, taking into account the close anatomical relationship between the large veins of the heart and the atrioventricular annuli [18], it can be assumed that during surgery for correcting the valvular heart disease, it is possible to change the anatomy of the venous bed of the heart, including that part that could be used as a target vein for the implantation of the LV lead. However, such a hypothesis was not evaluated in this study, which reduces the significance of the proposed explanation of the results.

An increase in the QRS interval duration on the surface ECG may reflect the degree of mechanical dyssynchrony, which, according to some authors, correlates directly with the probability of successful CRT [12, 19, 20]. In the present study, patients who responded positively to CRT had a longer QRS. This factor and the presence of the Strauss electrocardiographic criteria for LBBB were used as independent predictors of a decrease in LV ESV of ⩾ 15%.

Based on the analysis of computer models and data from electroanatomical mapping of the heart, the Strauss criteria, according to some researchers, have the best combination of sensitivity and specificity in predicting CRT response [21, 22]. The researchers explained the increase in the lower threshold of the QRS interval of ⩾130 ms in women and ⩾140 ms by the time required for the impulse to pass along the interventricular septum from the right ventricular endocardium to the LV endocardium and the subsequent spread of excitation and depolarization of the myocardium of the LV posterior lateral wall. This pattern of ventricular activation, characteristic of LBBB,

is also associated with the appearance of a double notch in lateral leads (V5, V6, I, aVL, and/or in V1 and V2) [14]. According to our findings, the verification of LBBB criteria according to Strauss increased the probability of a positive effect of CRT six times.

STUDY LIMITATIONS

This study is limited by its single-center setting. The developed model has not passed external validation, which limits its application in practice. The dynamics of LV ESV was assessed within 12 months after device implantation, and an increase in the follow-up period may increase the number of patients who responded to CRT.

CONCLUSION

The developed multivariate prognostic model may be useful in the selection of patients with CHF rEF for implantation of devices with CRT function. Among the parameters analyzed in the study, the Strauss electrocardiographic criteria for LBBB and QRS duration demonstrated an independent predictive potential to assess the probability of a positive hemodynamic response to CRT.

ADDITIONAL INFORMATION

Conflict of interest. The authors declare no conflict of interest.

REFERENCES

1. Polyakov DS, Fomin IV, Belenkov YuN, et al. Chronic heart failure in the Russian Federation: what has changed over 20 years of follow-up? Results of the EPOCH-CHF study. *Kardiologiia*. 2021;61(4):4–14. (In Russ.). DOI: 10.18087/cardio.2021.4.n1628

2. Ponikowski P, Voors AA, Anker SD, et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur J Heart Fail*. 2016;18(8):891–975. DOI: 10.1002/ejhf.592

3. Galand V, Singh JP, Heist EK. Can cardiac resynchronization therapy be used as a tool to reduce sudden cardiac arrest risk? *Prog Cardiovasc Dis*. 2019;62(3):242–248. DOI: 10.1016/j.pcad.2019.04.004

4. Ilov NN, Stompel DR, Palnikova OV, Nechepurenko AA. Echocardiography parameter for evaluation of various effects of cardiac resynchronization therapy. *Russian journal of cardiology and cardiovascular surgery*. 2022;15(1):19–25. (In Russ.). DOI: 10.17116/kardio20221501119

5. Russian Society of Cardiology (RSC). 2020 Clinical practice guidelines for Chronic heart failure. *Russian Journal of Cardiology*. 2020;25(11):4083. (In Russ.). DOI: 10.15829/1560-4071-2020-4083

6. McDonagh TA, Metra M, Adamo M, et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J*. 2021;42(36):3599–726. DOI: 10.1093/eurheartj/ehab368

7. Babukov RM, Popyl'kova OV, Bartosh FL, et al. Mitral leaflet coaptation depth as predictor of response to cardiac resynchronizing therapy. *Annali Aritmologii*. 2018;15(3):174–180. (In Russ.). DOI: 10.15275/annaritmol.2018.3.5

8. Shirokov NE, Kuznetsov VA, Soldatova AM, Krinochkin DV. Systolic thickening fraction of inerventricular septum as a predictor of superresponse to cardiac resyncronisation therapy - concept of a helical ventricular band. *Journal of Arrhythmology*. 2020;27(1):40–46. (In Russ.). DOI: 10.35336/VA-2020-1-40-46

9. Shlevkov NB, Gasparyan AZ, Zhambeev AA, et al. Soluble suppression of tumorigenesis-2 (sST2), a new potential biomarker of response to cardiac resynchronization therapy and cardiac contractility modulation in patients with chronic heart failure. *Almanac of Clinical Medicine*. 2021;49(2):99–112. (In Russ.). DOI: 10.18786/2072-0505-2021-49-025

10. Chairs TF, Daubert J-C, Saxon L, et al. 2012 EHRA/HRS expert consensus statement on cardiac resynchronization therapy in heart failure: implant and follow-up recommendations and management: A registered branch of the European Society of Cardiology (ESC), and the Heart Rhythm Society; and in col. *Europace*. 2012;14(9):1236–1286. DOI: 10.1093/europace/eus222

11. Covino G, Volpicelli M, Capogrosso P. Automatic Continuous CRT Optimization to Improve Hemodynamic Response: An Italian Single-Center Experience. *Int J Vasc Med*. 2020;2020:7942381. DOI: 10.1155/2020/7942381

12. Ilov NN, Surikova ON, Boytsov SA, et al. Possibilities for predicting ventricular tachyarrhythmias in patients with heart failure with reduced ejection fraction based on surface electrocardiography. First results from a single-center prospective study. *Russian Journal of Cardiology*. 2021;26(12):4661. (In Russ.). DOI: 10.15829/1560-4071-2021-4661

13. Ilov NN, Stompel DR, Boytsov SA, et al. Perspectives on the Use of Transthoracic Echocardiography Results for the Prediction of Ventricular Tachyarrhythmias in Pa-

tients with Non-ischemic Cardiomyopathy. *Rational Pharmacotherapy in Cardiology*. 2022;18(3):251–260. (In Russ.). DOI: 10.20996/1819-6446-2022-06-01

14. 1Strauss DG, Selvester RH, Wagner GS. Defining Left Bundle Branch Block in the Era of Cardiac Resynchronization Therapy. *Am J Cardiol*. 2011;107(6):927–934. DOI: 10.1016/j.amjcard.2010.11.010.

15. Leclercq C, Burri H, Curnis A, et al. Cardiac resynchronization therapy non- responder to responder conversion rate in the more response to cardiac resynchronization therapy with MultiPoint Pacing (MORE-CRT MPP) study : results from Phase I. *Eur Heart J*. 2019;40(35):2979–2987. DOI: 10.1093/eurheartj/ehz109

16. Gold MR, Rickard J, Daubert JC, et al. Redefining the Classifications of Response to Cardiac Resynchronization Therapy. *JACC Clin Electrophysio*. 2021;7(7):871–880. DOI: 10.1016/j.jacep.2020.11.010

17. Toro S, Tarakji K, Trulock K, et al. Reverse ventricular remodeling in patients with valvular heart disease undergoing cardiac resynchronization therapy. *J Am Coll Cardiol*. 2019;73(9-S1):418. DOI: 10.1016/S0735-1097(19)31026-5

18. Yap J, Bolling SF, Rogers JH. Contemporary Review in Interventional Cardiology: Mitral Annuloplasty in Secondary Mitral Regurgitation. *Struct Hear*. 2021;5(3):247–462. DOI: 10.1080/24748706.2021.1895457

19. Sweeney MO, van Bommel RJ, Schalij MJ, et al. Analysis of Ventricular Activation Using Surface Electrocardiography to Predict Left Ventricular Reverse Volumetric Remodeling During Cardiac Resynchronization Therapy. *Circulation*. 2010;121(5):626–634. DOI: 10.1161/CIRCULATIONAHA.109.894774

20. Poole JE, Singh JP, Birgersdotter-Green U. QRS Duration or QRS Morphology. *J Am Coll Cardiol*. 2016;67(9):1104–17. DOI: 10.1016/j.jacc.2015.12.039

21. van Deursen CJM, Blaauw Y, Witjens MI, et al. The value of the 12-lead ECG for evaluation and optimization of cardiac resynchronization therapy in daily clinical practice. *J Electrocardiol*. 2014;47(2):202–211. DOI: 10.1016/j.jelectrocard.2014.01.007

22. Kuznetsov VA, Malishevskii LM, Todosiychuk VV, Soldatova AM. Association of left bundle branch block definitions with response to cardiac resynchronisation therapy in patients with congestive heart failure. *Kardiologiia*. 2020;60(7):78–85. (In Russ.). DOI: 10.18087/cardio.2020.7.n785

СПИСОК ЛИТЕРАТУРЫ

1. Поляков Д.С., Фомин И.В., Беленков Ю.Н., и др. Хроническая сердечная недостаточность в Российской Федерации: что изменилось за 20 лет наблюдения? Результаты исследования ЭПОХА –ХСН // Кардиология. 2021. Т. 61, № 4. С. 4–14. DOI: 10.18087/cardio.2021.4.n1628

2. Ponikowski P., Voors A.A., Anker S.D., et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). Developed with the special contribution of the Heart Failure Association (HFA) of the ESC // Eur J Heart Fail. 2016. Vol. 18, No. 8. P. 891–975. DOI: 10.1002/ejhf.592

3. Galand V., Singh J.P., Heist E.K. Can cardiac resynchronization therapy be used as a tool to reduce sudden cardiac arrest risk? // Prog Cardiovasc Dis. 2019. Vol. 62, No. 3. P. 242–248. DOI: 10.1016/j.pcad.2019.04.004

4. Илов Н.Н., Стомпель Д.Р., Пальникова О.В., Нечепуренко А.А. Выбор эхокардиографического показателя для оценки разных эффектов сердечной ресинхронизирующей терапии // Кардиология и сердечно-сосудистая хирургия. 2022. Т. 15, № 1. С. 19–25. DOI: 10.17116/kardio20221501119

5. Терещенко С.Н., Галявич А.С., Ускач Т.М., и др. Хроническая сердечная недостаточность. Клинические рекомендации 2020 // Российский Кардиологический Журнал. 2020. Т. 25, № 11. С. 4083. DOI: 10.15829/1560-4071-2020-4083

6. McDonagh T.A., Metra M., Adamo M., et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure // Eur Heart J. 2021. Vol. 42, No. 36. P. 3599–726. DOI: 10.1093/eurheartj/ehab368

7. Бабуков Р.М., Попылькова О.В., Бартош Ф.Л., и др. Глубина коаптации створок митрального клапана как независимый предиктор ответа на ресинхронизирующую терапию // Анналы аритмологии. 2018. Т. 15, № 3. С. 174–180. DOI: 10.15275/annaritmol.2018.3.5

8. Широков Н.Е., Кузнецов В.А., Солдатова А.М., Криночкин Д.В. Систолическая фракция утолщения межжелудочковой перегородки как предиктор суперответа на сердечную ресинхронизирующую терапию – концепция спиральной желудочковой ленты // Вестник аритмологии. 2020. Т. 27, № 1. С. 40–46. DOI: 10.35336/VA-2020-1-40-46

9. Шлевков Н.Б., Гаспарян А.Ж., Жамбеев А.А., и др. Растворимый рецептор подавления туморогенности второго типа (sST2) – новый потенциальный биомаркер положительных результатов применения сердечной ресинхронизирующей терапии и модуляции сердечной сократимости у больных хронической сердечной недостаточностью // Альманах

клинической медицины. 2021. Т. 49, № 2. С. 99–112. DOI: 10.18786/2072-0505-2021-49-025

10. Chairs T.F., Daubert J.-C., Saxon L., et al. 2012 EHRA/HRS expert consensus statement on cardiac resynchronization therapy in heart failure: implant and follow-up recommendations and management: A registered branch of the European Society of Cardiology (ESC), and the Heart Rhythm Society; and in col // Europace. 2012. Vol. 14, No. 9. P.1236–1286. DOI: 10.1093/europace/eus222

11. Covino G., Volpicelli M., Capogrosso P. Automatic Continuous CRT Optimization to Improve Hemodynamic Response: An Italian Single-Center Experience // Int J Vasc Med. 2020. Vol. 2020. ID 7942381. DOI: 10.1155/2020/7942381

12. Илов Н.Н., Сурикова О.Н., Бойцов С.А., и др. Возможности прогнозирования риска возникновения желудочковых тахиаритмий у больных хронической сердечной недостаточностью со сниженной фракцией выброса левого желудочка на основе анализа поверхностной электрокардиограммы. Первые результаты одноцентрового проспективного исследования // Российский кардиологический журнал. 2021. Т. 26, № 12. С. 4661. DOI: 10.15829/1560-4071-2021-4661

13. Илов Н.Н., Стомпель Д.Р., Бойцов С.А., и др. Перспективы использования результатов трансторакальной эхокардиографии для прогнозирования желудочковых тахиаритмий у больных неишемической кардиомиопатией // Рациональная Фармакотерапия в Кардиологии. 2022. Т. 18, № 3. С. 251–260. DOI: 10.20996/1819-6446-2022-06-01

14. Strauss D.G., Selvester R.H., Wagner G.S. Defining Left Bundle Branch Block in the Era of Cardiac Resynchronization Therapy // Am J Cardiol. 2011. Vol. 107, No. 6. P. 927–934. DOI: 10.1016/j.amjcard.2010.11.010.

15. Leclercq C., Burri H., Curnis A., et al. Cardiac resynchronization therapy non- responder to responder conversion rate in the more response to cardiac resynchronization therapy with MultiPoint Pacing (MORE-CRT MPP) study : results from Phase I // Eur Heart J. 2019. Vol. 40, No. 35. P. 2979–2987. DOI: 10.1093/eurheartj/ehz109

16. Gold M.R., Rickard J., Daubert J.C., et al. Redefining the Classifications of Response to Cardiac Resynchronization Therapy // JACC Clin Electrophysio. 2021. Vol. 7, No. 7. P. 871–880. DOI: 10.1016/j.jacep.2020.11.010

17. Toro S., Tarakji K., Trulock K., et al. Reverse ventricular remodeling in patients with valvular heart disease undergoing cardiac resynchronization therapy // J Am Coll Cardiol. 2019. Vol. 73, No. 9-S1. P. 418. DOI: 10.1016/S0735-1097(19)31026-5

18. Yap J., Bolling S.F., Rogers J.H. Contemporary Review in Interventional Cardiology: Mitral Annuloplasty in Secondary Mitral Regurgitation // Struct Hear. 2021. Vol. 5, No. 3. P. 247–462. DOI: 10.1080/24748706.2021.1895457

19. Sweeney M.O., van Bommel R.J., Schalij M.J., et al. Analysis of Ventricular Activation Using Surface Electrocardiography to Predict Left Ventricular Reverse Volumetric Remodeling During Cardiac Resynchronization Therapy // Circulation. 2010. Vol. 121, No. 5. P. 626–634. DOI: 10.1161/CIRCULATIONAHA.109.894774

20. Poole J.E., Singh J.P., Birgersdotter-Green U. QRS Duration or QRS Morphology // J Am Coll Cardiol. 2016. Vol. 67, No. 9. P. 1104–17. DOI: 10.1016/j.jacc.2015.12.039

21. van Deursen C.J.M., Blaauw Y., Witjens M.I., et al. The value of the 12-lead ECG for evaluation and optimization of cardiac resynchronization therapy in daily clinical practice // J Electrocardiol. 2014. Vol. 47, No. 2. P. 202–211. DOI: 10.1016/j.jelectrocard.2014.01.007

22. Кузнецов В.А., Малишевский Л.М., Тодосийчук В.В., Солдатова А.М. Оценка взаимосвязи различных критериев блокады левой ножки пучка Гиса с ответом на сердечную ресинхронизирующую терапию при хронической сердечной недостаточности // Кардиология. 2020. Т. 60, № 7. С. 78–85. DOI: 10.18087/cardio.2020.7.n785

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Research article

Differential Diagnostics of Wide QRS Complex Arrhythmias with Left Bundle Branch Block Morphology Using Slow Conduction Index

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Differential diagnosis of wide QRS complex arrhythmias is one of the most challenging tasks in routine practice arrhythmology. The analysis of the wide QRS complex morphology has been introduced due to the complex problem of detecting atrial waves on ECG. A slow conduction index based on the ratio of the initial and terminal QRS amplitudes is one of the solutions to evaluate conduction velocity based on the surface ECG due to a significant variability of QRS morphology and real complexity of its detailed assessment. However, one of the significant limitations of this algorithm is a need to search for the RS wide complex type and randomly select an ECG lead with this morphology which can finally create a contradictory result.

AIM: To evaluate a possibility of using the slow conduction index for differential diagnosis of wide QRS complex arrhythmias with left bundle branch (LBBB) morphology in any of 12-leads ECG followed by evaluation of the obtained diagnostic accuracy values.

MATERIALS AND METHODS: The study included 280 single premature wide QRS complexes with LBBB morphology recorded during holter ECG monitoring in randomly selected 28 patients. Atrial extrasystoles were recorded in 14 patients and ventricular extrasystoles were captured during sinus rhythm in other 14 patients. A ROC analysis was used for the qualitative and quantitative assessment of a slow conduction index diagnostic values based on sensitivity (Sn), specificity (Sp) and accuracy (Acc).

RESULTS: The highest values of Sn and Sp were obtained for a slow conduction index in the leads aVL, V2, aVF, V5 and III, and the lowest — for the leads I, V3 and V6 based on the calculated area (AUC) under the ROC curves ($p < 0.001$ for all leads).

CONCLUSION: The study presented the fundamental possibility of using a slow conduction index in any of 12-lead ECG for the differential diagnosis of wide QRS complex arrhythmias with LBBB morphology.

Keywords: differential diagnosis; wide QRS complex; left bundle branch block.

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Научная статья

Использование индекса медленного проведения в дифференциальной диагностике аритмий с широкими комплексами QRS и формой блокады левой ножки пучка Гиса

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Актуальность. Дифференциальная диагностика аритмий с широкими комплексами QRS является одной из сложнейших задач в практической аритмологии. В связи со сложностью выявления волн предсердной активности на ЭКГ часто используется подход, основанный на анализе формы комплекса QRS. Учитывая выраженную вариабельность формы QRS и сложность объективной оценки, было предложено оценивать на ЭКГ скорость распространения возбуждения по миокарду желудочков на основе так называемого индекса медленного проведения — соотношения амплитуд начальной и конечной частей комплекса QRS. Однако одним из существенных ограничений данного алгоритма является необходимость не только искать отведения с формой широкого комплекса по типу RS, но и произвольно выбирать такое отведение при наличии нескольких похожих, что может приводить к противоречивым результатам.

Цель исследования — изучение возможности использования индекса медленного проведения для дифференциальной диагностики аритмий с широкими комплексами QRS и формой блокады левой ножки пучка Гиса (ЛНПГ) во всех 12 отведениях ЭКГ с последующей оценкой его диагностической значимости.

Материалы и методы. В исследование было включено 280 одиночных преждевременных широких комплексов QRS с формой блокады ЛНПГ, выявленных при односуточном и многосуточном мониторировании ЭКГ у случайно выбранных 28 пациентов. У 14 больных регистрировались предсердные экстрасистолы и у 14 — желудочковые экстрасистолы во время синусового ритма. Для качественной и количественной оценки диагностической значимости использовался ROC-анализ с определением информативности диагностического теста на основании чувствительности (ЧВ), специфичности (СП) и диагностической точности (ДТ).

Результаты. Наиболее высокие значения ЧВ и СП индекса медленного проведения для широких комплексов QRS были получены в отведениях aVL, V2, aVF, V5 и III, а наиболее низкие — в отведениях I, V3 и V6 согласно анализу рассчитанной площади (AUC) под ROC кривыми ($p < 0{,}001$ для всех отведений).

Заключение. В проведенном исследовании была показана принципиальная возможность использования индекса медленного проведения для дифференциальной диагностики аритмий с широкими комплексами QRS и формой блокады ЛНПГ в любом отведении ЭКГ.

Ключевые слова: дифференциальная диагностика; широкие комплексы QRS; блокада левой ножки пучка Гиса.

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BACKGROUND

The differential diagnosis of wide QRS complex arrhythmias is one of the most difficult scientific and practical tasks in electrocardiology and noninvasive arrhythmology. For more than 60 years, this problem remains unresolved to the end; however, it is still very relevant: cardiologists and specialists in functional diagnostics constantly face the need to differentiate wide QRS tachyarrhythmias in their daily practical work because competent analysis in most cases determines successful therapeutic techniques [1, 2].

The main principle of the differential diagnosis of wide QRS arrhythmias is the analysis of electrocardiograms (ECGs) and the identification of atrial activities and their detailed assessment in relationship with the QRS complex. However, in most cases, it is impossible to clearly visualize the P waves on surface ECG because of their small amplitudes and frequent locations in the ST-T interval when premature ventricular complexes appear. In some cases, when atrial flutter or fibrillation occurs, it is impossible to reliably determine which waves of the atrial electrical activity are conducted to the ventricles.

In all these cases, a different principle based on the analysis of the form of wide QRS complexes should be used. Many scientific groups have developed and proposed various morphological criteria and algorithms for the differential diagnosis of wide QRS arrhythmias [3]. Most of them are based on the assessment of amplitudes and time parameters of wide QRS complexes in leads V1 and V6 [4–7]. Moreover, other authors have shown low diagnostic accuracy (Acc) [8]. This is caused by the high subjectivity of the assessment of the shape of the wide QRS by researchers and the heterogeneity of patient groups, some of whom could have structural changes in the heart. Scar or intense myocardial fibrosis leads to a significant change in the course of excitation along the ventricular myocardium and, accordingly, to a sharp decrease in the diagnostic capabilities of these algorithms [9]. In addition, a significant difference in individual anatomical ratios of the torso and the position of the heart in the chest is an important factor, which also has significant effects on the QRS complex morphology.

One of the approaches to solve these problems is an ECG assessment of the propagation rate of excitations through the ventricular myocardium based on the ratio of the amplitudes of the initial and final parts of the QRS complex. Thus, in 2006, Vereckei et al. proposed the so-called slow conduction index for the differential diagnosis of wide QRS arrhythmias [10]. The slow conduction index is the ratio of the absolute values of the total amplitude of the QRS complex for the first and last 40 ms, which is calculated for a single ECG lead. If the obtained value is < 1, the wide QRS complex has a ventricular origin, and if it is > 1, it is supraventricular (Figure 1). The evaluation results of the diagnostic significance of the proposed criterion showed quite good results: sensitivity (Sn) of 88.2% and specificity (Sp) of 81.9% [10].

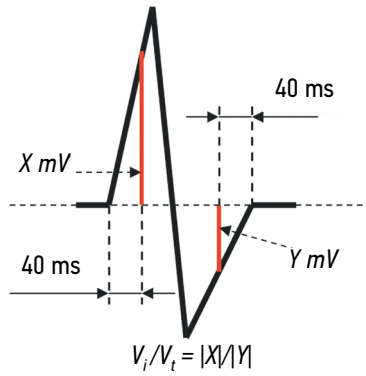

Fig. 1. A method of determining the amplitudes during the initial ($V_i = X\ mV$) and terminal ($V_t = Y\ mV$) 40 ms of QRS complex and slow conduction index calculation ($V_i / V_t = X / Y$).

Furthermore, the special feature of this index is the need to choose an ECG lead with the RS-type wide complex according to the original concept of the proposed criterion. However, this is one of the significant limitations of this algorithm: the need not only to specifically look for leads with the RS-type wide complex but also to arbitrarily choose one of such leads from among several similar ones, which can give contradictory results. In addition, the absence of the RS-type complex shape leads to the failure to use the slow conduction index in practice.

In this regard, this study aimed to analyze the possibility of using this criterion in all 12 ECG leads for the differential diagnosis of wide QRS complex arrhythmias with left bundle branch block (LBBB) morphology, followed by the assessment of the obtained values for its diagnostic significance.

MATERIALS AND METHODS

Data registration

The study included 280 single premature wide QRS complexes with LBBB morphology identified during 1-day and multiday ECG monitoring in 28 randomly selected patients undergoing hospital treatment at the FSBI Almazov National Medical Research Centre of the Ministry of Healthcare of the Russian Federation from 2010 to 2019. ECG registration was conducted using standard isoline filters, with 35 and 50 Hz, and recording with a sampling frequency of 257 Hz (INCART CJSC, Russia). In all patients, signs of additional conduction pathways or initial bundle branch block were excluded. The diagnosis of ventricular or supraventricular arrhythmias was verified by experts (cardiologists and functional diagnostics specialists) by comparing ECG data with the results of the endocardial electrophysiological examination and by analyzing the ratio of the atrial and ventricular rates under clear visualization of the P waves before the occurrence of premature wide QRS complexes on the surface and transesophageal ECG. Atrial premature

beats were recorded in 14 patients and ventricular premature beats during the sinoatrial rate in 14 patients. ECG samples of patients with ventricular and supraventricular arrhythmias with the shape of the complex forming an LBBB are shown in Figures 2 and 3, respectively.

Data processing

For all wide QRS complexes (*N* = 280) in each of the 12 leads, the QRS complex borders were determined automatically using the KTResult 3 software (INCART CJSC, Russia). The correctness of their automatic determination was

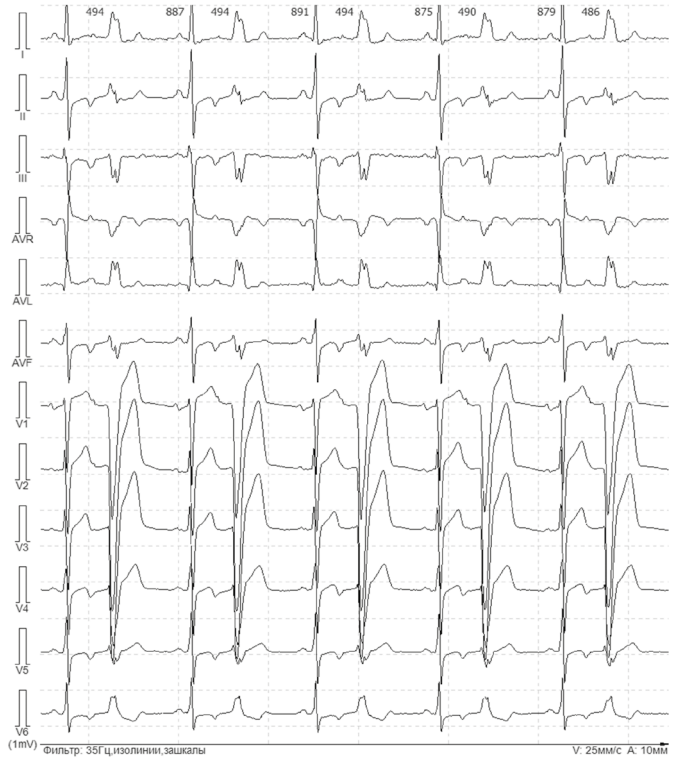

Fig. 2. ECG example of supraventricular extrasystoles with LBBB aberration

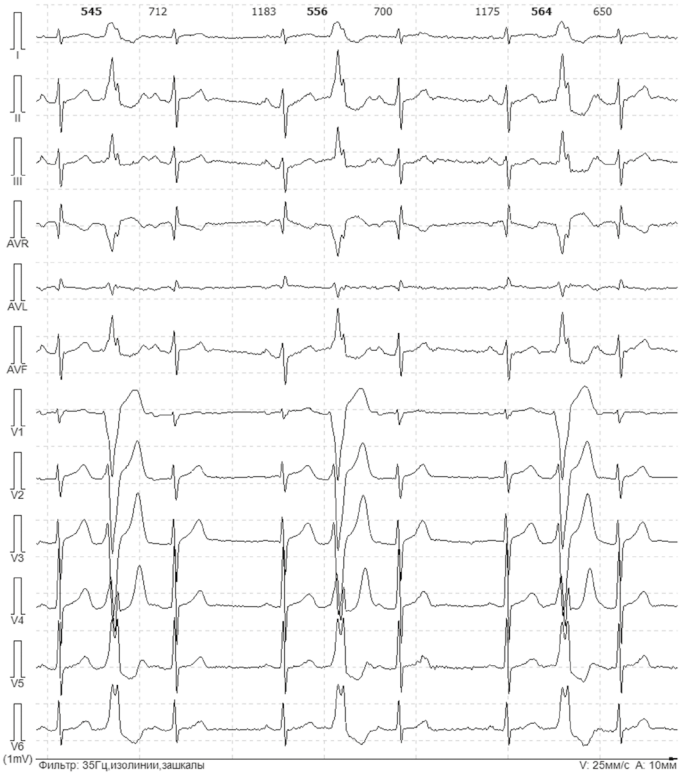

Fig. 3. ECG example of ventricular extrasystoles with LBBB type morphology

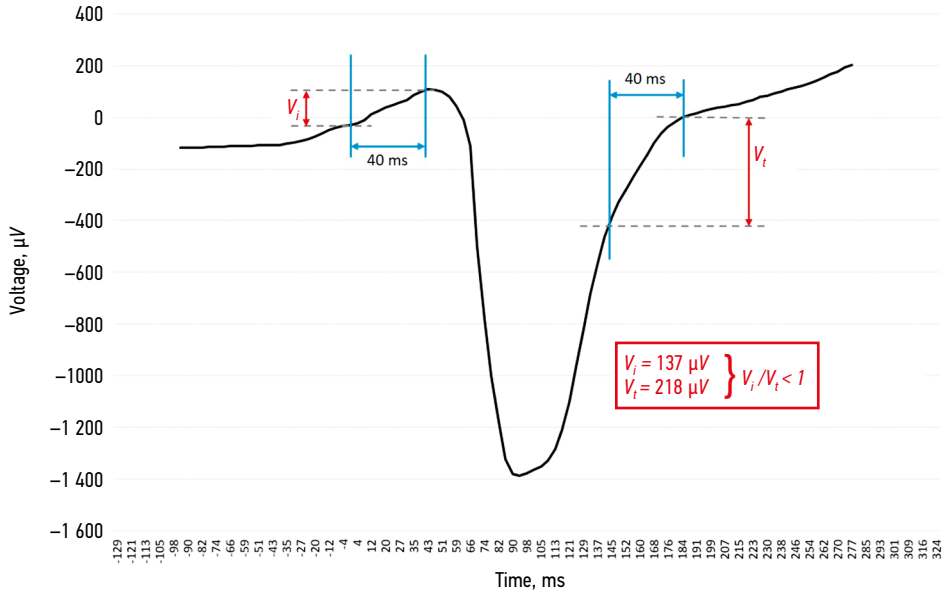

Fig. 4. An example of slow conduction index calculation (V_i/V_t). Voltage (μ*V*) — ECG amplitude (microVolts), time in ms

checked by an expert (a doctor of functional diagnostics), who conducted subsequent corrections if necessary. The obtained amplitude–time parameters for the first and last 40 ms of all QRS complexes were exported from the KTResult 3 software in text format using custom-made software based on the Embarcadero RAD Studio v.10.2 rapid application development environment (Idera Inc., USA) and imported into Microsoft Excel spreadsheets (Microsoft Corporation). Then, the ratio of the absolute values of the total amplitudes of the QRS complexes for the first and last 40 ms in each ECG lead was calculated. Absolute values of amplitude deviations were used for monophase complexes. In the case of a two- or three-phase complex, the sum of the amplitudes of these deviations during the initial or final 40 ms was used. The technique and example of determining the amplitudes and calculation of the slow conduction index are shown in Figure 4.

Statistical analysis

In the first stage, the nature of the data distribution was evaluated using histograms, normal probability plots, Shapiro–Wilk test [11] modified by Royston [12], and the generalized D'Agostino-Pearson test [13]. Initially, p values < 0.05 were assumed to be statistically significant. All data obtained significantly differed from the normal distribution; therefore, nonparametric methods of analysis were used.

In the second stage, a receiver operating characteristic (ROC) analysis was performed [14; 15] to qualitatively and quantitatively assess the diagnostic significance of the slow conduction index and characteristics of premature ventricular contractions (PVC) and supraventricular (premature atrial complexes [PAC]). ROC curves were made separately for each indicator, followed by a detailed analysis of their shape. The areas under the curve (AUCs) were compared based on the values of the standard error calculated using the Hanley and McNeil method [16, 17] and the exact 95% confidence interval (CI) based on the binomial distribution [18]. The informative value of the diagnostic test was based on the calculated values of Sn, Sp, and diagnostic Acc. The Sn, Sp, and Acc were assessed with their 95% CI calculated based on the binomial distribution using the Klopper–Pearson method [19, 20].

Considering that several hypotheses were tested simultaneously using the same set of initial data in this study, the probability of making an incorrect conclusion about at least one of the hypotheses significantly exceeded the initially accepted significance level (p < 0.05). Thus, the Bonferroni adjustment factor was used to adjust the obtained values for multiple testing [21], and p values < 0.001 were considered finally statistically significant. Statistical analysis was performed using Statistica v.12 (Statsoft Inc., USA), IBM SPSS Statistics for Windows version 23 (IBM Corp., Armonk, NY, USA), and MedCalc Statistical Software v.20.115 (MedCalc Software Ltd, Ostend, Belgium).

RESULTS

Clinical characteristics of the patients

The patients were 10 to 76 years old (median, 43 years); among them, 17 (61%) were male. Coronary heart disease (CHD) was diagnosed in 3 patients, hypertension in 6, and chronic heart failure functional class 2 (NYHA) in 2. Echocardiography showed left ventricular hypertrophy in 9 patients (5 with PVC and 4 with PAC) and dilated cardiomyopathy of nonischemic origin in 3 (1 with PVC and 2 with PAC).

Sn and Sp analysis of the slow conduction index in 12 ECG leads

The highest Sn and Sp values of the slow conduction index were obtained in leads aVL, V2, aVF, V5, and III and the lowest in leads I, V3, and V6 according to the analysis of the AUC under the ROC curves. Moreover, a statistically significant difference was noted in all leads (p < 0.001),

even in leads with low AUC values. The calculated CI was quite narrow in all leads. All the obtained values are presented in Table. In the evaluation of the diagnostic value of the QRS shape, AUC did not exceed 0.83 in any of the leads. The shape of the ROC curve together with their 95% CI and cut-off threshold criteria for each ECG lead are shown in Figure 5.

Diagnostic Acc of the slow conduction index in 12 ECG leads

In the evaluation of the diagnostic Acc of the slow conduction index, none of the leads obtained values exceeding 94%. A visual comparison of the diagnostic Acc of the slow conduction index in different ECG leads showed that leads aVL, V2, aVF, V5, and III were the most informative for the differential diagnosis in order of descending of their value (Figure 6). The range of 95% CI for diagnostic Acc values was relatively narrow for the slow conduction index in each ECG lead.

DISCUSSION

Main results

This study explored the possibility of using the slow conduction index for the differential diagnosis of wide QRS

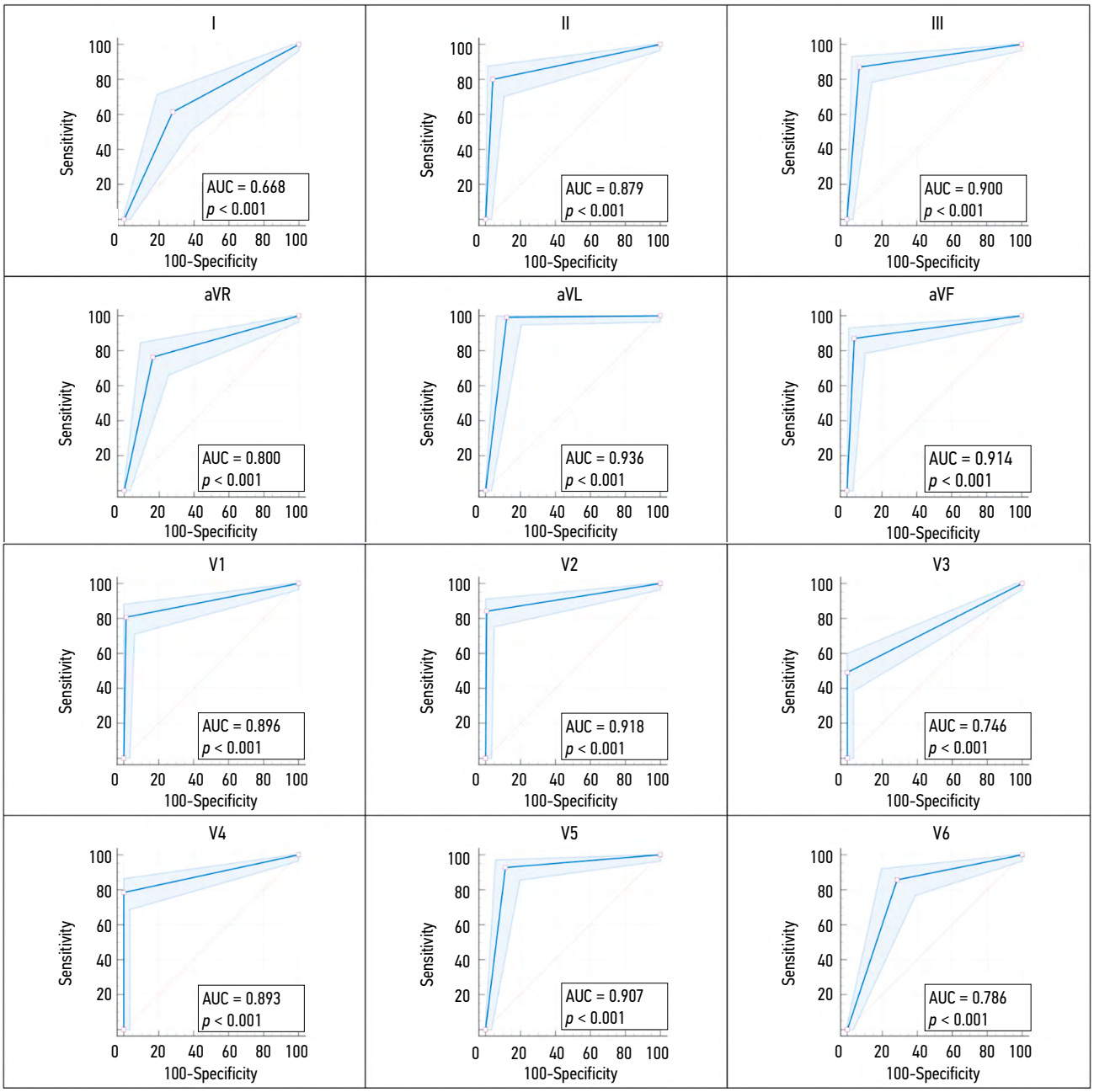

Fig. 5. ROC curves with 95% CI (light blue color) as an illustration of diagnostic value of slow conduction index in 12 lead ECG. Cut-off values are marked as red round marker on each of ROC curves. Area under curve (AUC) with *p*-value are shown at the right bottom corner of each graph

Table. Diagnostic characteristics (Sn, Sp and AUC with 95% CI) of slow conduction index in 12-lead ECG

Lead	Sn (95% CI), %	Sp (95% CI), %	AUC (95% CI)
I	61.4 (53–70)	72.1 (64–79)	0.67 (0.61–0.72)
II	80.0 (72–86)	95.7 (91–98)	0.88 (0.83–0.91)
III	87.1 (80–92)	92.9 (87–97)	0.90 (0.86–0.93)
aVR	76.4 (69–83)	83.6 (76–89)	0.80 (0.75–0.85)
aVL	99.3 (96–100)	87.9 (81–93)	0.94 (0.90–0.96)
aVF	87.1 (80–92)	95.7 (91–98)	0.91 (0.88–0.94)
V1	80.7 (73–87)	98.6 (95–100)	0.90 (0.86–0.93)
V2	84.3 (77–90)	99.3 (96–100)	0.92 (0.88–0.95)
V3	49.3 (41–58)	100 (97–100)	0.75 (0.69–0.80)
V4	78.6 (71–85)	100 (97–100)	0.89 (085–0.93)
V5	92.9 (87–97)	88.6 (82–93)	0.91 (0.87–0.94)
V6	85.7 (79–91)	71.4 (63–79)	0.79 (0.73–0.83)

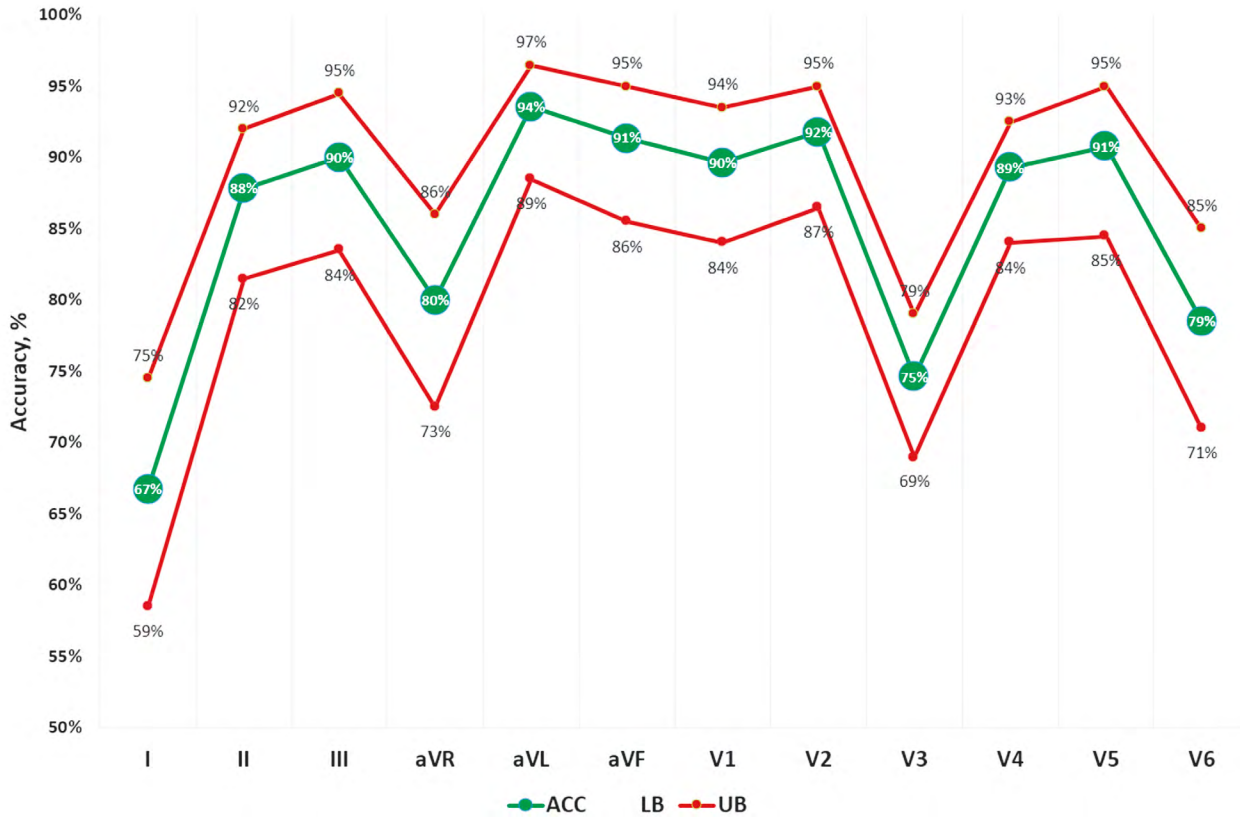

Fig. 6. Line plot of slow conduction index Accuracy (Acc) with 95% CI in all 12 leads. LB-UB – lower bound-upper bound of 95% CI.

arrhythmias with the shape of an LBBB in all 12 ECG leads and assessed the calculated values of diagnostic significance. The obtained results showed the potential for use of this criterion in any of the ECG lead without the need to search for a biphasic wide complex with an RS-type morphology. In addition, the calculated diagnostic Acc showed high Sn and Sp of the slow conduction index in leads II, III, aVL, aVF, V1, V2, V4, and V5 (8 of 12). These results are confirmed by

the fact that the area under the ROC curves was statistically significant ($p < 0.001$) in all leads, even in leads with low AUC values.

In the visual comparison of the diagnostic Acc of the slow conduction index in all leads, a significant advantage was found when this criterion was used in eight of the above leads, whereas when used in only in four leads (I, aVR, V3, and V6), the Acc was lower.

Diagnostic value of the slow conduction index and evaluation of the results relative to previously published data

The analysis of the wide QRS complexes morphology for the differential diagnosis of ventricular and supraventricular arrhythmias appears to be more relevant than the analysis of the ratio of atrial and ventricular rhythms for several reasons. First, in most cases, it is impossible to detect the presence of AV dissociation because of the small amplitude of the atrial P waves on the ECG, which makes this criterion extremely difficult to use in clinical practice. Second, even when atrial activity waves are found, further detailed analysis of the ratios of the atrial and ventricular rhythm is required. Finally, most often, doctors just do not have the time to search for atrial waves on an ECG and conduct further detailed ECG analysis. In addition, the analysis of the amplitude–time characteristics of wide complexes also appears to be a very complicated task because of the abundance of proposed criteria and algorithms, most of which take into account only one or several morphological criteria of wide QRS complexes.

The criteria of differential diagnosis of the wide complexes with LBBB morphology in the available literature were previously described mainly for the duration of the QRS complex or for leads V1, V2, and V6 [7, 22, 23], rarely for leads I and AVF [24], and are not described for leads V3 and V4. Criteria such as R duration of > 30 ms, notch of the descending part of the S-wave, distance from the beginning of the QRS complex to the maximum peak of the S-wave ⩾ 70 ms in leads V1 and V2, or presence of any Q-wave in lead V6 had high diagnostic Acc according to many studies [7, 22–24]. Thus, according to Kindall, Brown, and Josephson, it was not possible to differentiate VT and SVT with an Acc of 96%–100% [23], and according to Griffith and de Belder, the Acc was only 74% (86%) for patients with CHD and 60% for those without CHD) [24]. However, no large-scale study has assessed their Acc for arrhythmias with LBBB morphology, and for arrhythmias with any form of QRS complex, the Acc was only 73% for the AVF lead and 60% for the I lead [24].

The development of criteria for the differential diagnosis of arrhythmias with wide QRS complexes is complicated because of various reasons. Initially, the ECG characteristics are largely influenced by many factors: position of the heart in the chest, characteristics of the conductivity of the myocardium and surrounding tissues, electrical potential of skeletal muscles, and characteristics of the transient resistance between the skin surface and registration electrodes, which can change significantly based on their displacement and deterioration of their contact. These factors can significantly influence the QRS complexes morphology; thus, their variability can be very intense even for long-term ECG registration in one patient. In this regard, the correct selection of criteria based on the analysis of the amplitude–time parameters of QRS becomes very important. From among all the currently proposed criteria for the differential diagnosis of arrhythmias with wide QRS complexes, the slow conduction index, from our point of view, is the most suitable for describing the complex process of excitation along the ventricular myocardium. However, this index should be only used in leads with a biphasic or three-phase shape of the wide complex, most often of the RS type, which significantly complicates the diagnosis. Moreover, in the original works of the authors regarding this criterion, this was not clearly explained. Later, the authors suggested using this criterion only for the aVR lead [25]. In practical work, if there is a need to use the slow conduction index for the differential diagnosis of ventricular and supraventricular arrhythmias with wide QRS complexes, any data confirming the potential for use of any ECG leads suitable for analysis from the point of view of a specialist should be available.

In this paper, the diagnostic significance of the slow conduction index does not directly depend on the selection of a lead with a biphasic or three-phase shape of the wide QRS complex. Moreover, in most leads, the use of the slow conduction index showed high Sn, Sp, and Acc. A detailed analysis of the calculated ROC curves showed the presence of a relatively narrow 95% CI, which may indirectly indicate the low variability of the diagnostic value of parameters and their robustness.

Our study showed the potential for use of the slow conduction index in patients with wide complexes and shape of an LBBB, when the differential diagnosis is difficult because of the abundance and difficulty of using other morphological criteria [26]. Of course, the results cannot be a strict pattern identified; thus, additional analysis and verification in a much larger group of patients without structural cardiac disease are needed.

Assessment of the representativeness and study limitations

The study analyzed a relatively small number of arrhythmias with wide QRS complexes; thus, the results may be highly specific for the studied patients. In addition, the use of nonparametric ROC analysis with the calculation of 95% CI significantly increased the robustness of the obtained results. Possible errors in automatic ECG measurement and potential registration errors associated with the registration of artifacts may affect the results, which together with the small sample size can limit the generalizability of this study. Moreover, the consistency and systematicity of the conducted analysis in relation

to the analysis methods used significantly increase the reliability and representativeness of the results.

CONCLUSION

The study showed the potential use of the slow conduction index in the differential diagnosis of arrhythmias with wide QRS complexes in any of ECG leads. In patients with LBBB QRS morphology, the best results of the diagnostic Acc of this index were obtained in leads II, III, aVL, aVF, V1, V2, V4, and V5. Thus, in this study, the use of the slow conduction index in different ECG leads does not depend on the shape of the QRS complex and not only complements but also significantly improves the quality of the differential diagnosis of PVC and PAC with aberrant conduction of LBBB. Given the small sample size, the obtained results require further testing on a larger group of patients with different forms of wide ectopic complexes with LBBB morphology and different localizations of ventricular arrhythmia focus, taking into account the presence of cardiac structural disease.

The study also demonstrated the importance of a comprehensive approach in the analysis of the QRS complex morphology and the need for a consistent detailed analysis of various criteria for the differential diagnosis of arrhythmias with wide QRS complexes.

ADDITIONAL INFORMATION

Competing interests. Conflict of interest. The authors declare no potential conflict of interest.

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REFERENCES

1. Abedin Z. Differential diagnosis of wide QRS tachycardia: A review. *J Arrhythm*. 2021;37(5):1162-1172. DOI:10.1002/joa3.12599.

2. Медведев ММ. Дифференциальная диагностика тахикардий с широкими комплексами QRS: от «классических» признаков к первым алгоритмам. Вестник аритмологии. 2019;26(3):48-56. DOI:10.35336/VA-2019-3-48-56.

3. Alzand BSN, Crijns HJGM. Diagnostic criteria of broad QRS complex tachycardia: decades of evolution. *Europace*. 2011;13(4):465-472. DOI:10.1093/europace/euq430.

4. Brugada P, Brugada J, Mont L, Smeets J, Andries EW. A new approach to the differential diagnosis of a regular tachycardia with a wide QRS complex. *Circulation*. 1991;83(5):1649-1659. DOI:10.1161/01.cir.83.5.1649.

5. Kim M, Kwon CH, Lee JH, et al. Right bundle branch block-type wide QRS complex tachycardia with a reversed R/S complex in lead V6: Development and validation of electrocardiographic differentiation criteria. *Heart Rhythm*. 2021;18(2):181-188. DOI:10.1016/j.hrthm.2020.08.023.

6. Chen Q, Xu J, Gianni C, et al. Simple electrocardiographic criteria for rapid identification of wide QRS complex tachycardia: The new limb lead algorithm. *Heart Rhythm*. 2020;17(3):431-438. DOI:10.1016/j.hrthm.2019.09.021.

7. Drew BJ, Scheinman MM. ECG Criteria to Distinguish Between Aberrantly Conducted Supraventricular Tachycardia and Ventricular Tachycardia:Practical Aspects for the Immediate Care Setting. *Pacing Clin Electro*. 1995;18(12):2194-2208. DOI:10.1111/j.1540-8159.1995.tb04647.x.

8. May AM, Brenes-Salazar JA, DeSimone CV, et al. Electrocardiogram algorithms used to differentiate wide complex tachycardias demonstrate diagnostic limitations when applied by non-cardiologists. *J Electrocardiol*. 2018;51(6):1103-1109. DOI:10.1016/j.jelectrocard.2018.09.015.

9. Медведев ММ, Парижский АБ. Почему «не работают» электрокардиографические алгоритмы дифференциальной диагностики тахикардий с широкими комплексами QRS. Вестник аритмологии. 2020;27(2):54-66. DOI:10.35336/VA-2020-2-54-66.

10. Vereckei A, Duray G, Szenasi G, Altemose GT, Miller JM. Application of a new algorithm in the differential diagnosis of wide QRS complex tachycardia. *Eur Heart J*. 2007;28(5):589-600. DOI:10.1093/eurheartj/ehl473.

11. Shapiro SS, Wilk MB. An Analysis of Variance Test for Normality (Complete Samples). *Biometrika*. 1965;52(3/4):591. DOI:10.2307/2333709.

12. Royston P. A Toolkit for Testing for Non-Normality in Complete and Censored Samples. *Journal of the Royal Statistical Society. Series D (The Statistician)*. 1993;42(1):37-43. http://www.jstor.org/stable/2348109. Accessed December 2, 2022.

13. Sheskin D. *Handbook of parametric and nonparametric statistical procedures*. 5th ed. Boca Raton: CRC Press; 2011.

14. Metz CE. Basic principles of ROC analysis. *Semin Nucl Med*. 1978;8(4):283-298. DOI:10.1016/s0001-2998(78)80014-2.

15. Zweig MH, Campbell G. Receiver-operating characteristic (ROC) plots: a fundamental evaluation tool in clinical medicine. *Clin Chem*. 1993;39(4):561-577.

16. Hanley JA, McNeil BJ. The meaning and use of the area under a receiver operating characteristic (ROC) curve. *Radiology*. 1982;143(1):29-36. DOI:10.1148/radiology.143.1.7063747.

17. Hanley JA, Hajian-Tilaki KO. Sampling variability of nonparametric estimates of the areas under receiver operating characteristic curves: an update. *Academic Radiology*. 1997;4(1):49-58. DOI:10.1016/s1076-6332(97)80161-4.

18. Hilgers RA. Distribution-free confidence bounds for ROC curves. *Methods Inf Med*. 1991;30(2):96-101.

19. Clopper CJ, Person ES. The use of confidence or fiducial limits illustrated in the case of the binomial. *Biometrika*. 1934;26(4): 404-413. DOI:10.1093/biomet/26.4.404.
20. 20. Krishnamoorthy K, Peng J. Some Properties of the Exact and Score Methods for Binomial Proportion and Sample Size Calculation. *Communications in Statistics – Simulation and Computation*. 2007;36(6):1171-1186. DOI:10.1080/03610910701569218.
21. Dunn OJ. Multiple Comparisons among Means. *Journal of the American Statistical Association*. 1961;56(293):52-64. DOI:10.1080/01621459.1961.10482090.
22. Wellens HJ, Brugada P, Wellens HJ, Brugada P. Diagnosis of ventricular tachycardia from the 12-lead electrocardiogram // Diagnosis of Ventricular Tachycardia from the 12-Lead Electrocardiogram. *Cardiology clinics*. 1987;5(3):511-525. DOI:10.1016/s0733-8651(18)30538-1.
23. Kindwall KE, Brown J, Josephson ME. Electrocardiographic criteria for ventricular tachycardia in wide complex left bundle branch block morphology tachycardias. *Am J Cardiol*. 1988;61(15):1279-1283. DOI:10.1016/0002-9149(88)91169-1.
24. Griffith JM, Belder AM de, Linker JN, et al. Multivariate analysis to simplify the differential diagnosis of broad complex tachycardia. *British Heart Journal*. 1991;66(2):166-174. DOI:10.1136/hrt.66.2.166.
25. Vereckei A, Duray G, Szénási G, Altemose GT, Miller JM. New algorithm using only lead aVR for differential diagnosis of wide QRS complex tachycardia. *Heart Rhythm*. 2008;5(1):89-98. DOI:10.1016/j.hrthm.2007.09.020.
26. Griffith MJ, Belder MA de, Linker NJ, Ward DE, Camm AJ. Difficulties in the use of electrocardiographic criteria for the differential diagnosis of left bundle branch block pattern tachycardia in patients with a structurally normal heart. *Eur Heart J*. 1992;13(4):478-483. DOI:10.1093/oxfordjournals.eurheartj.a060200.

СПИСОК ЛИТЕРАТУРЫ

1. Abedin Z. Differential diagnosis of wide QRS tachycardia: A review // Journal of arrhythmia. 2021. 37. № 5. С. 1162–1172. DOI: 10.1002/joa3.12599.
2. Медведев М.М. Дифференциальная диагностика тахикардий с широкими комплексами QRS: от «классических» признаков к первым алгоритмам // Вестник аритмологии. 2019. 26. № 3. С. 48–56. DOI: 10.35336/VA-2019-3-48-56.
3. Alzand B.S.N., Crijns H.J.G.M. Diagnostic criteria of broad QRS complex tachycardia: decades of evolution // Europace : European pacing, arrhythmias, and cardiac electrophysiology : journal of the working groups on cardiac pacing, arrhythmias, and cardiac cellular electrophysiology of the European Society of Cardiology. 2011. 13. № 4. С. 465–472. DOI: 10.1093/europace/euq430.
4. Brugada P., Brugada J., Mont L., Smeets J., Andries E. W. A new approach to the differential diagnosis of a regular tachycardia with a wide QRS complex // Circulation. 1991. 83. № 5. С. 1649–1659. DOI: 10.1161/01.cir.83.5.1649.
5. Kim M., Kwon C.H., Lee J.H., Hwang K.W., Choi H.O., Kim Y.-G., Lee K.-N., Ahn J., Park H.-S., Nam G.-B. Right bundle branch block-type wide QRS complex tachycardia with a reversed R/S complex in lead V6: Development and validation of electrocardiographic differentiation criteria // Heart rhythm. 2021. 18. № 2. С. 181–188. DOI: 10.1016/j.hrthm.2020.08.023.
6. Chen Q., Xu J., Gianni C., Trivedi C., Della Rocca D.G., Bassiouny M., Canpolat U., Tapia A.C., Burkhardt J. D., Sanchez J.E., Hranitzky P., Gallinghouse G.J., Al-Ahmad A., Horton R., Di Biase L., Mohanty S., Natale A. Simple electrocardiographic criteria for rapid identification of wide QRS complex tachycardia: The new limb lead algorithm // Heart rhythm. 2020. 17. № 3. С. 431–438. DOI: 10.1016/j.hrthm.2019.09.021.
7. Drew B.J., Scheinman M.M. ECG Criteria to Distinguish Between Aberrantly Conducted Supraventricular Tachycardia and Ventricular Tachycardia:Practical Aspects for the Immediate Care Setting // Pacing and Clinical Electrophysiology. 1995. 18. № 12. С. 2194–2208. DOI: 10.1111/j.1540-8159.1995.tb04647.x.
8. May A.M., Brenes-Salazar J.A., DeSimone C.V., Vaidya V.R., Ternus B.W., Hodge D. O., Lin G., Mulpuru S. K., Deshmukh A.J., Noseworthy P.A., Brady P.A. Electrocardiogram algorithms used to differentiate wide complex tachycardias demonstrate diagnostic limitations when applied by non-cardiologists // Journal of electrocardiology. 2018. 51. № 6. С. 1103–1109. DOI: 10.1016/j.jelectrocard.2018.09.015.
9. Медведев М. М., Парижский А. Б. Почему «не работают» электрокардиографические алгоритмы дифференциальной диагностики тахикардий с широкими комплексами QRS // Вестник аритмологии. 2020. 27. № 2. С. 54–66. DOI: 10.35336/VA-2020-2-54-66.
10. Vereckei A., Duray G., Szenasi G., Altemose G.T., Miller J.M. Application of a new algorithm in the differential diagnosis of wide QRS complex tachycardia // European heart journal. 2007. 28. № 5. С. 589–600. DOI: 10.1093/eurheartj/ehl473.
11. Shapiro S.S., Wilk M.B. An Analysis of Variance Test for Normality (Complete Samples) // Biometrika. 1965. 52. 3/4. С. 591. DOI: 10.2307/2333709.
12. Royston P.A Toolkit for Testing for Non-Normality in Complete and Censored Samples // Journal of the Royal Statistical Society. Series D (The Statistician). 1993. 42. № 1. С. 37–43.
13. Sheskin D. Handbook of parametric and nonparametric statistical procedures. 5-е изд. Boca Raton: CRC Press, 2011. xxxix,1886.
14. Metz C.E. Basic principles of ROC analysis // Seminars in nuclear medicine. 1978. 8. № 4. С. 283–298. DOI: 10.1016/s0001-2998(78)80014-2.
15. Zweig M. H., Campbell G. Receiver-operating characteristic (ROC) plots: a fundamental evaluation tool in clinical medicine // Clinical chemistry. 1993. 39. № 4. С. 561–577.
16. Hanley J.A., McNeil B.J. The meaning and use of the area under a receiver operating characteristic (ROC) curve // Radiology. 1982. 143. № 1. С. 29–36. DOI: 10.1148/radiology.143.1.7063747.

17. Hanley J.A., Hajian-Tilaki K.O. Sampling variability of nonparametric estimates of the areas under receiver operating characteristic curves: an update // Academic Radiology. 1997. 4. № 1. С. 49–58. DOI: 10.1016/s1076-6332(97)80161-4.
18. Hilgers R.A. Distribution-free confidence bounds for ROC curves // Methods of information in medicine. 1991. 30. № 2. С. 96–101.
19. Clopper C.J., Person E. S. The use of confidence or fiducial limits illustrated in the case of the binomial // Biometrika. 1934. 26. № 4. С. 404–413. DOI: 10.1093/biomet/26.4.404.
20. Krishnamoorthy K., Peng J. Some Properties of the Exact and Score Methods for Binomial Proportion and Sample Size Calculation // Communications in Statistics - Simulation and Computation. 2007. 36. № 6. С. 1171–1186. DOI: 10.1080/03610910701569218.
21. Dunn O.J. Multiple Comparisons among Means // Journal of the American Statistical Association. 1961. 56. № 293. С. 52–64. DOI: 10.1080/01621459.1961.10482090.
22. Wellens H.J., Brugada P., Wellens H.J., Brugada P. Diagnosis of ventricular tachycardia from the 12-lead electrocardiogram // Diagnosis of Ventricular Tachycardia from the 12-Lead Electrocardiogram // Cardiology clinics. 1987. 5. № 3. С. 511–525. DOI: 10.1016/s0733-8651(18)30538-1.
23. Kindwall K.E., Brown J., Josephson M.E. Electrocardiographic criteria for ventricular tachycardia in wide complex left bundle branch block morphology tachycardias // The American journal of cardiology. 1988. 61. № 15. С. 1279–1283. DOI: 10.1016/0002-9149(88)91169-1.
24. Griffith J.M., Belder A.M. de, Linker J.N., Ward D.E., Camm A. John, Griffith M.J., Belder M.A. de, Linker N.J., WARD D.E., Camm A.J. Multivariate analysis to simplify the differential diagnosis of broad complex tachycardia // British Heart Journal. 1991. 66. № 2. С. 166–174. DOI: 10.1136/hrt.66.2.166.
25. Vereckei A., Duray G., Szénási G., Altemose G.T., Miller J.M. New algorithm using only lead aVR for differential diagnosis of wide QRS complex tachycardia // Heart rhythm. 2008. 5. № 1. С. 89–98. DOI: 10.1016/j.hrthm.2007.09.020.
26. Griffith M.J., Belder M.A. de, Linker N.J., Ward D.E., Camm A.J. Difficulties in the use of electrocardiographic criteria for the differential diagnosis of left bundle branch block pattern tachycardia in patients with a structurally normal heart // European heart journal. 1992. 13. № 4. С. 478–483. DOI: 10.1093/oxfordjournals.eurheartj.a060200.

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ЭКО • ВЕКТОР

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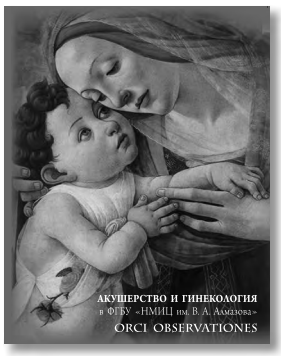
ОСНОВЫ АНЕСТЕЗИОЛОГИИ И РЕАНИМАТОЛОГИИ

НОВИНКА

ЭВОЛЮЦИЯ ПРЕДИКТИВНОЙ МЕДИЦИНЫ
Под ред. В.С. Баранова

Ферри Фред Ф., Багненко С.Ф.

СПРАВОЧНИК ПАЦИЕНТА ПО ФЕРРИ



АКУШЕРСТВО И ГИНЕКОЛОГИЯ В ФГБУ «НМИЦ ИМ. В.А. АЛМАЗОВА» ORCI OBSERVATIONES
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Max Solomonovich Kushakovsky. Life and work

Yuri N. Grishkin

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

Born on 1 December 1922 in the small Ukrainian town of Zvenigorodka, Cherkasy region; died on 11 Juni 2002 in Saint Petersburg.

In 1947, M.S. Kushakovky graduated from the Military Medical Academy with merits, and his name was among the first to be put on Academy's marble plaque of honor after the war. At the beginning of 1951, M.S. Kushakovky defended his PhD. thesis on the topic “Hemodynamic disorders and the condition of the precapillary bed in advanced stages of hypertension (on the issue of adaptive mechanisms)”. In September 1960 he received the academic title of Associate Professor. At the department, he was in charge of the clinical department, conducted practical classes with students of the 3rd and 6th years of the Military Medical Academy, lectured for military doctors of advanced courses on various sections of internal diseases, functional diagnostics of diseases of the heart and blood vessels. In 1965, the doctoral dissertation was successfully defended. In total, he published 17 monographs (including reprints) and more than 220 articles. Max Solomonovich was a member of the editorial boards of the journals Arterial Hypertension and Bulletin of Arrhythmology. For a long time, Max Solomonovich was a board member of the therapeutic and cardiological societies of Leningrad and St. Petersburg. Prof. M.S. Kushakovsky was a scientific advisor for 30 PhD students. In 2001, he was awarded the title of "Honorary Doctor" of the St. Petersburg Medical Academy of Postgraduate Education, as well as the title of "Honorary Cardiologist of Russia".

In 2003, the Department of Cardiology of St. Petersburg Medical Academy of Postgraduate Education was named after him. Since 2011, after the merger of St. Petersburg Medical Academy of Postgraduate Education and Leningrad Sanitary and Hygienic Medical Institute, the combined Department of Hospital Therapy and Cardiology has born his name.

Keywords: personalities; biography; history of medicine; cardiology.

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Макс Соломонович Кушаковский. Жизнь и деятельность

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Макс Соломонович Кушаковский родился 1 декабря 1922 года в небольшом украинском городке Звенигородка, Черкасской области; умер 11 июня 2022 г в Санкт Петербурге.

В 1947 г. М.С. Кушаковский окончил Военно-Медицинскую Академию с золотой медалью, и его фамилия была в числе первых курсантов, имена которых были занесены на мраморную доску почета Академии после войны. В начале 1951 г. М.С. Кушаковский защитил кандидатскую диссертацию на тему «Нарушения гемодинамики и состояние прекапиллярного русла в далеко зашедших стадиях гипертонической болезни (к вопросу о приспособительных механизмах)».

В сентябре 1960 г. М.С. Кушаковский получил ученое звание доцента. На кафедре М.С. Кушаковский заведовал клиническим отделением, вел практические занятия со слушателями 3-го и 6-го курсов Военно-медицинской академии, читал лекции для военных врачей курсов усовершенствования по разным разделам внутренних болезней, функциональной диагностике заболеваний сердца и сосудов. В 1965 состоялась защита докторской диссертации.

Всего М.С. Кушаковским было опубликовано 17 монографий (учитывая переиздания) и более 220 статей. Макс Соломонович являлся членом редакционных советов журналов «Артериальная гипертензия» и «Вестник аритмологии». Длительное время Макс Соломонович был членом правления терапевтического и кардиологического обществ Ленинграда и Санкт-Петербурга. Под научным руководством проф. М.С. Кушаковского были выполнены и защищены 5 докторских и 25 кандидатских диссертаций. В 2001 году он был удостоен звания «Почетного доктора» Санкт-Петербургской медицинской Академии последипломного образования, а также звания «Почетный кардиолог России». В 2003 г. его имя было присвоено кафедре кардиологии СПб МАПО, а с 2011 г, после слияния СПб МАПО и ЛСГМИ его имя носит объединенная кафедра госпитальной терапии и кардиологии.

Ключевые слова: персоналии; биография; история медицины; кардиология

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On the first winter day of December 1922, in the small Ukrainian town of Zvenigorodka, Cherkasy region, a son was born to the Kushakovsky family. He was named Max. He was the first and, as it turned out later, the only child. His father Solomon Todrosovich Kushakovsky (1887–1978), also from Zvenigorodka, began his career as a joiner's apprentice, then worked at a furniture factory. From 1917 he worked in various elected party bodies. Max's mother Tulchinskaya Bronislava Markovna (1898-1984) was a housewife.

Max grew up as a healthy and intelligent boy. He spent his childhood in Zvenigorodka, where he went to school and completed the first three grades. In 1933, the Kushakovsky family moved to the city of Vinnitsa due to a new appointment of his father as the head of the party archive. Max went to school number 18, graduating in 1940 with merits. On the advice of his father, he planned to enter a medical school, but there was a Finnish war at that time, and the country was restless. In July 1940, he was examined by the Vinnitsa Conscription Commission that declared him fit for military service but also dismissed him to "leave to arrange household chores until September 15, 1940". In September 1940, he was drafted into the army and served as a soldier in the 524th regiment in the town of Shuya, Ivanovo Region. Instead of lectures on medicine, classes, tests and exams, he had to comprehend artillery science.

From the very first days of the war, Max Kushakovsky joined the army as part of the 696th artillery regiment that fought on the Western Front. Month of heavy fighting, retreat from the western border of the country... On July 22, 1941, his regiment entered the battle with a tank column of the Nazis on the Sozh River near the Belarusian city of Propoisk. The commander of the anti-tank arms, Sergeant Kushakovsky, together with his crew, fought to the last. Everyone died, he was seriously wounded. He woke up only in a field medical hospital, deployed in the dense forests of Bryansk, where he was taken to by PO-2 plane. There, he underwent several difficult operations to remove several hundred fragments, although doctors failed to remove them all. From August 30 to October 27, 1941, he was on rehabilitation in the evacuation hospital in Stalingrad. The certificate issued upon discharge from the hospital read: "Multiple shrapnel wounds to the face, upper jaw, torso".

After the end of treatment, he was granted a leave for 30 days in the city of Orenburg until December 1941. Even though the medical commissions at that time did not really "nitpick" about the consequences of injuries during re-examination, Sergeant Kushakovsky was still declared unfit for military service. The commission granted his request to be appointed as a hospital porter (anyway, closer to medicine), and then he served in the Chkalov evacuation hospital until mid — 1942.

Although the war continued in the country, the government decided to send a group of veterans to the Military Medical Academy. In the fall of 1942 Sergeant M.S. Kushakovsky passed the entrance exam in chemistry

Fig. 1. Max Solomonovich Ushakovsky (1922–2002)

Fig. 2. Solomon Todrosovich Kushakovsky (1887–1978), Tulchinskaya Bronislava Markovna (1898-1984)

Fig. 3. Last days in school.

(it was then the main subject) with excellent marks and was admitted to the Kuibyshev Military Medical Academy, which at that time was evacuated to the city of Chkalov. However, soon Kuibyshev Academy was disbanded. Cadet Kushakovsky, as a front-line soldier who suffered a severe wound, was transferred to the Leningrad Military Medical Academy, located in the city of Samarkand. The dormitories of the academy were as crowded as soldier's barracks.

Fig. 4. Pencil portrait 1941

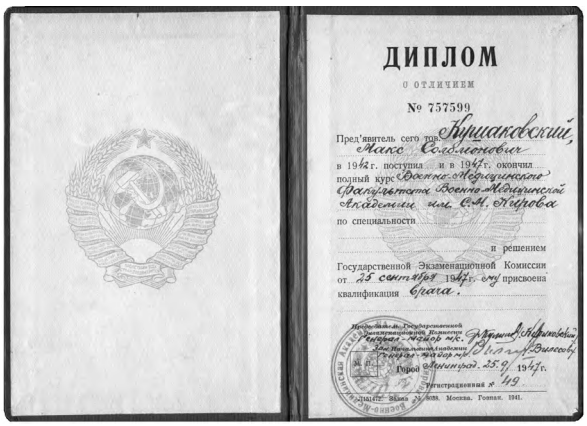
ДИПЛОМ
С ОТЛИЧИЕМ
№ 757599
Предъявитель сего тов. Кушаковский, Макс Соломонович в 1942 г. поступил и в 1947 г. окончил полный курс Военно-Медицинского Факультета Военно-Медицинской Академии им. С.М. Кирова по специальности
и решением Государственной Экзаменационной Комиссии от 23 сентября 1947 г. ему присвоена квалификация Врача.
Город Ленинград 25/9 1947 г.
Зарегистрированный № 49

Fig. 5. Diplom of Military Medical Academy with merits

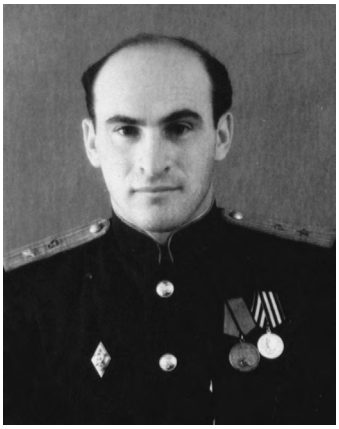

Fig. 6. Krasnovodsk. Head of the therapeutic department 1954

There was not enough food, Uzbek vegetables and fruits were of some help. There was no news from relatives who were under occupation. However, none of Max's classmates ever heard a single complaint from him. On the contrary, yesterday's front-line soldier who celebrated his twentieth birthday in a hot Central Asian city cheered up his friends himself.

After the blockade of Leningrad was lifted in 1944, teachers and cadets of the Military Medical Academy returned to Leningrad. Education process continued. They lived in the dormitory of the Academy on Botkinskaya street. The cadet Kushakovsky was one of the best in his course, having only excellent marks in the record. Organized, self-disciplined, he was for a long time the prefect of the course, and then the commander of the training group of 30 listeners. In 1947, he graduated from the Military Medical Academy with merits, and his name was among the first to be put on Academy's marble plaque of honor after the war.

As the best graduate, he was given the opportunity to apply for postgraduate studies. In October 1947, he passed the entrance exams and was admitted to the postgraduate course at the Department of Propaedeutics of Internal Diseases, which at that time was headed by Academician of the Academy of Medical Sciences Professor N.N. Savitsky. M.S. Kushakovsky was committed to investigate the peculiarities of hemodynamic disorders in patients with hypertension. The work went well, the first two scientific articles were published, and at the beginning of 1951 he defended his PhD. thesis on the topic "Hemodynamic disorders and the condition of the precapillary bed in advanced stages of hypertension (on the issue of adaptive mechanisms)".

At the end of the postgraduate course, M.S. Kushakovsky continued his academic activity at the department of propaedeutics of internal diseases as a teacher. However, the young scientist believed that practical experience was vital for his further work. Having worked as a teacher for only half a year — until June 1951, he filed a report on transfer to the hospital, and was soon appointed a doctor at army hospital No. 943, located in Krasnovodsk (Turkmenistan). There he served as head of the therapeutic department for 4 years.

From the very first days of his work, Max Solomonovich proved himself to be an excellent clinician, possessing a very wide range of special clinical knowledge and an extraordinary ability for fine diagnostic analysis. There was a lot of work, and living conditions were not easy: an unusual climate, heat, sandstorms. However, Captain M.S. Kushakovsky, spending most of his time in the hospital, provided medical assistance to local fishermen, ship repairers, Nebit-Dag oil workers, and shepherds. Often, he was invited to lecture at the local medical school. It was in Krasnovodsk, he had decided on the topic of a doctoral dissertation, and he was still actively engaged in scientific work.

In December 1955, being in the rank of major, M.S. Kushakovsky was dismissed from the army due to the consequences of being wounded. In February 1956, he again returned to the Department of Propaedeutics of Internal Diseases of the Military Medical Academy, where he first worked as an intern and then as an assistant. In September 1960 he received the academic title of Associate Professor. At the department, he was in charge of the clinical department, conducted practical classes with students of the 3rd and 6th years of the Military Medical Academy, lectured for military

doctors of advanced courses on various sections of internal diseases, functional diagnostics of diseases of the heart and blood vessels. There he met Elena Ivanova Dorokhova, who also taught at the department and later became his life partner for many years.

For a long time, he lived in a dormitory, because he could not register in Leningrad in any way. Professors N.N. Savitsky and Z.M. Volynsky helped to solve the problem with registration. After their visit to the chairman of the City Executive Committee, Max Solomonovich was finally registered in the city, and so he became a Leningrader.

Besides teaching, all these years he was engaged in the problems of methemoglobinemia, which was closely connected with the emergence of nuclear weapons, radiation damage and radioprotective agents. During the years of work on his dissertation, he published a whole series of papers on this topic and continued studies of hypertension. Vast experimental material, as well as his clinical observations, formed the basis of his doctoral dissertation "Methemoglobinemia and the emergence of other pathological derivatives of hemoglobin. Finding new means of treatment and prevention (clinical and experimental study)". The dissertation turned out to be very large (770 pages of text!), and comprised two volumes. As Max Solomonovich recalled, all official opponents showed obvious dissatisfaction when seeing this two-volume book. However, in 1965 the doctoral dissertation was successfully defended. On March 5, 1966 M.S. Kushakovsky was awarded the degree of Doctor of Medical Sciences.

Since 1967, professional activities of M.S. Kushakovsky took place in the State Institute of Professional Development of Physicians named after V.I. Lenin. Professor I.I. Isakov, who was then the head of the Department of Therapy No. 2, knowing Max Solomonovich well from their joint work in the therapeutic section of the Leningrad Society of Cardiology, invited him to the post of professor of the department (the academic title "Professor" was awarded to Max Solomonovich in 1968). The transition process was not easy at all. The Chairman of the Presidium of the Leningrad Scientific Society of Therapists, Academician N.S. Molchanov, chairman of the cardiology section of the society, professor A.A. Kedrov, Academician N.N. Savitsky petitioned for M.S. Kushakovsky appointment. On September 29, 1967, the Academic Council of the State Institute Professional Development of Physicians named after V.I. Lenin "recognized him as worthy of being elected to the position of professor of the Department of Therapy II" (out of 42 members of the Council, 37 voted in favor and 5 voted against).

A new stage in the life of Max Solomonovich began. He gave new lectures at all cycles conducted by the department on a wide range of issues in both therapy and cardiology. Fantastic memory, excellent knowledge of theory and extensive clinical experience were the basis for profound and extraordinary lectures in many respects. This brought great satisfaction to the listeners of the cycles, and also gradually began to attract city specialists. M.S. Kushakovsky's clinical rounds, conducted with students of cycles of further education, clinical residents and hospital doctors, deserved no less attention. Being meticulous himself, he demanded the same from his students. On the rounds, he constantly forced the doctors to percuss and auscultate the patients. Possessing absolute hearing and using a metal stethoscope (which no one else used except for him), during auscultation of the heart, he heard things that no one else could hear (at one time he was called "the third tone").

Recalling the years of training in clinical residency, one of the residents (now the chief therapist of a vast region in the Far East) said that from time to time the residents were knocked sideways by M.S. Kushakovsky's questions. However, he would never tell department staff or the cadet doctors off. When something didn't suit him (for example, the lack of an answer to a question asked, or, moreover, an incorrect answer), he would sigh, shake his head reproachfully and state, "But you need to know this!". Sometimes, in response to a tricky question about an unusual clinical situation, after a short reflection, he would remark melancholy "It happens" (in the department this phrase has long become a household word). And one could be absolutely sure that it is very rare, but it happens. Often this was followed by an example from his own practice, sometimes from many years ago, but, nevertheless, the exact picture of the disease was recalled, and sometimes even the patient's name.

At the same time, Max Solomonovich immediately had to fulfill a lot of other departmental duties: conducting a philosophical seminar, which was obligatory at that time, socialist competition, together with prof. I.I. Isakov, he was engaged in the scientific work of the department. Postgraduate courses began. At the same time, he took an active part in the planning of the cardiological building under construction at Hospital No. 1. A huge burden lay on his shoulders while combining work on the board of the Leningrad Society of Cardiology, duties in the problematic commission on cardiovascular pathology, etc. After the retirement of Prof. I.I. Isakov in 1974 Max Solomonovich became the head of the department of cardiology (since 1969).

Max Solomonovich devoted his entire life to science and practical healthcare. His first published scientific work was the abstract for the Military Healthcare Academy scientific conference in 1950 named "Hemodynamic disorders and the condition of the capillary bed in advanced stages of hypertension." Issues of etiology, pathogenesis, development of modern methods of diagnosis and treatment of arterial hypertension were his research purposes. Between 1950 and 1960 alone, he published 15 articles and theses devoted to these problems.

Work at the Military Medical Academy entailed a scientific search in the field of development and application of radioprotective agents for radiation sickness. 26 papers were devoted to this issue (as well as works closed for wide public access) and published in journals "Biochemistry",

"Medical Radiology", "Bulletin of the USSR Academy of Medical Sciences", etc. At the same time, M.S. Kushakovsky developed another problem that was connected mainly with methemoglobinemia. The result of this work, in addition to his doctoral dissertation, was his first monograph "Clinical forms of damage to hemoglobin", published by the publishing house "Medicina" in 1968 with a circulation of 10 000 copies. The book contained a lot of new data in this field of knowledge (e.g., a new direction in clinical medicine was suggested — "hemoglobinology").

While working for the Department of Therapy No. 2 of State Institute of Professional Development for Physicians named after V. I. Lenin, and then for the Department of Cardiology, Professor M.S. Kushakovsky had a great interest in the problems of cardiac arrhythmias and conduction. He used to write, this was largely due to his great impression of the book by B. Hoffman and P. Cranefield "Electrophysiology of the Heart" (1962). Kushakovsky's first works on this topic appeared in 1970, and no later than in 1972 a textbook for cadets on clinical electrocardiography was published. It was fundamentally different from the existing works on this topic, and is very popular among doctors even today. In 1972, joint monograph "Selected Issues of Clinical Electrocardiography" was published, where M.S. Kushakovsky wrote a section on cardiac arrhythmias and conduction disorders. In 1974, monograph "Clinical electrocardiography" was published (republished in 1984). Later it received a diploma of the Prize of the USSR Academy of Medical Sciences named after A.L. Myasnikov.

Another area of interest for Prof. M.S. Kushakovsky was myocardial dystrophy. A significant part of this work was carried out jointly with Prof. L.A. Butchenko. Joint monographs "Myocardial dystrophy in athletes" (1980) and "Adaptive changes in the cardiovascular system of athletes with different orientations of the training process" (1982) were published.

In 1977, monograph "Hypertension" was published soon highly recognized among doctors. Further work on the problem of arterial hypertension allowed Max Solomonovich to issue five more editions of this book, each time substantially revised and supplemented. The latest edition of Essential Hypertension (2002) was published a week before his death. His "Atlas of Electrocardiograms. Arrhythmias and heart blocks", written together with N.B. Zhuravleva is also highly recognized. The monograph was awarded the prize of Russian Medical Academy named after G.F. Lang and has been reprinted three more times.

In his last years of life, Prof. M.S. Kushakovsky published monographs "Chronic heart failure. Idiopathic cardiomyopathies" (1997), "Heart arrhythmias (2nd edition, 1998), "Atrial fibrillation" (1999), "Arrhythmias and heart block. Atlas of electrocardiograms" (1999), "Metabolic heart disease" (2000). In total, he published 17 monographs (including reprints) and more than 220 articles. Max Solomonovich was a member of the editorial boards of the journals Arterial Hypertension and Bulletin of Arrhythmology. For a long time, Max Solomonovich was a board member of the therapeutic and cardiological societies of Leningrad and St. Petersburg.

Prof. M.S. Kushakovsky was a scientific advisor for 30 PhD students. Dissertation topics were usually proposed by Max Solomonovich himself, based either on his own scientific interests or on promising scientific directions. In this sense, his imagination source was inexhaustible, since he read everything that had been written and was available for reading. Not being able to speak any foreign language (except Ukrainian), he nevertheless was able to understand

Fig. 7. Head Department of Cardiology prof. M.S. Kushakovsky with teachers, graduate students and clinical residents.1981

German and English-language scientific literature. It was hard to walk around in his home. Books were everywhere — sitting in bookcases, on tables, on furniture and on the floor. It was difficult to understand how he navigated through this ocean of books and magazines.

Being his graduate student was not easy. Having brought another chapter or article, you could be sure that the next morning you would get it back with so many edits that your own text was no longer seen. Max Solomonovich did not change his habit of writing all texts by hand until the end of his life. He never used a typewriter, and, unlike many, he never accepted the computer. However, with age, as is usually the case with doctors, his handwriting remained practically unchanged, being as clear and understandable as before. Moreover, his handwritten page matched the standard sizes for a typewritten sheet, which also made it easier for his graduate students and editors of his numerous monographs. Sometimes instead of his/her own, a graduate student would receive a completely new text fully rewritten by hand by Max Solomonovich. But there were never any complaints about this. Unobtrusively, but constantly, he would check how research was being done, how records were being kept. It is characteristic that sometimes he knew the work of his students better than they themselves. In his books and articles, whenever an opportunity presented itself, he would always refer to these works.

It was extremely interesting to talk to Max Solomonovich outside work. This was a rare occasion, mainly during offsite courses. His interests were broad, and not at all limited to science. He was very fond of sports, although he himself was never particularly involved in it. He was interested in chess, figure skating, hockey and many other sports. However, his passion was football. He never missed interesting matches, and during the world championships, his attention was definitely occupied by football. In the morning, his first question would be "Did you watch the match yesterday?" followed by bewilderment on his face, if the answer was negative. He knew all the players, the results of the matches and is believed to would have been an excellent sports commentator.

Max Solomonovich always preferred classical music and was a regular at the Philharmonic's concert hall. He knew perfectly all the operas and ballets given in our theaters, the main soloists. He always tried to get to the premieres. His favorite reading was art albums, the information from which was firmly embedded in his memory. His favorite writers were Dickens, Turgenev and Leo Tolstoy. Knowing their works perfectly well, he would often quote excerpts from them, adding a picture to life situations.

While on offsite course, he tried every possible way to replenish his knowledge about the history of these places. In the towns of Ivanovo, Pskov, Novgorod, Sochi he would participate in tours with great interest, listened to the guides most attentively. In the end, it seemed to us that the guide was not needed at all, because in his absence Max Solomonovich could tell no less. In Novgorod, he could talk for hours about the temples we examined, about the history of the Rublevsky frescoes. In the Pskov-Pechersk Lavra, we enjoyed lectures on the history of religion. In the museum of Dostoevsky, we (in addition to the guide) heard from Max Solomonovich a lot of details from the life of the writer himself and his characters. So it was, always and everywhere.

In everyday life, he was extremely undemanding, and didn't treat down-to-earth problems seriously. But, since, as he himself said, driving in a nail was an issue for him, some difficulties arose in everyday life. He had neither a summer

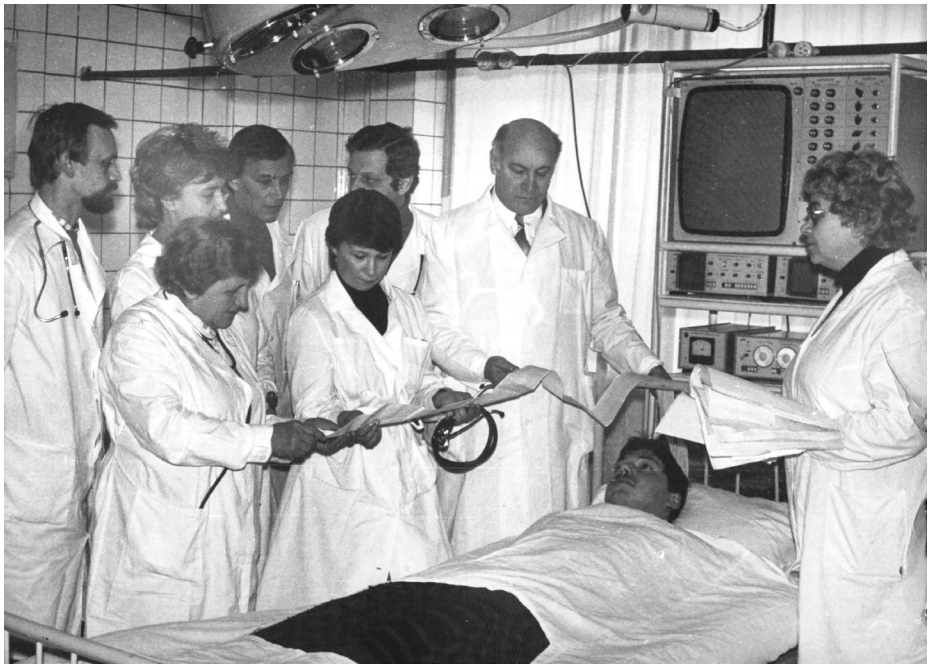

Fig. 8. Consultations in the intensive care unit of the city antiarrhythmic center at hospital No. 1. 1981


ПРЕЗИДИУМ АКАДЕМИИ МЕДИЦИНСКИХ НАУК
СОЮЗА СОВЕТСКИХ СОЦИАЛИСТИЧЕСКИХ РЕСПУБЛИК
в заседании своем от 7 декабря 1977 г.
ПРИСУДИЛ
профессору
Кушаковскому Максу Соломоновичу
с соавторами
Диплом именной премии
имени А.Л.Мясникова
За монографию „Клиническая
электрокардиография", Ленинград, 1974 г.
г. МОСКВА, 1978 г.

Fig. 9. Diploma of the A.L. Myasnikov 1978


ВСЕРОССИЙСКОЕ НАУЧНОЕ
ОБЩЕСТВО КАРДИОЛОГОВ
ПОЧЕТНЫЙ КАРДИОЛОГ РОССИИ
Кушаковский
Макс Соломонович
За заслуги в развитии
кардиологической науки
и организации
кардиологической службы
Президент ВНОК Р. Г. Оганов
Генеральный секретарь С. А. Шальнова

Fig. 10. Diploma of the title "Honorary Cardiologist of Russia" 2001

house nor a car. He did not know how to drive a car, and he never aspired to do so. The ear piece that fell off the glasses became a burning problem immediately, since reading was no longer possible. An urgent repair of glasses using a paper clip and a compass could temporarily improve the situation. Next, he was advised to go to the workshop and install a new screw. However, after some time, the second ear piece fell off. Inspection showed that that the paper clip performed its functions properly, and then the next one was used.

Having suffered a serious illness in 1982, Max Solomonovich had to take hormonal drugs for a long time, which, as a result, led to the development of arthrosis of the hip joint. In a sense, we probably contributed to this by putting a bicycle ergometer in his office and forcing him to use it regularly. This made life somewhat difficult, though he himself took the problem philosophically. Before the illness he used to get to the hospital by metro, and then walk from the metro station "Vasileoostrovskaya" to the department for about 3 km. On the way he was reading all the newspapers that were on the stands of Bolshoy Prospekt (according to his classmate and friend, D. I. Tsank, he developed this habit back in his student years). After the illness however he had to get to work by taxi. In the Soviet times it was affordable but after the monetary reform of the 90s, his salary was barely enough for this. Nevertheless, his working schedule remained the same, the management of the Pokrovskaya hospital also helped with transport. The transfer to half-time job as a professor of the department made it possible to travel to Vasilyevsky Island less often, but it did not change anything in the way of life. There was more time for working with literature and for publishing monographs. After the death, several manuscripts of his articles were found, as well as the monograph "Arrhythmias of the Heart", which increased in size several times and was jam-packed with bookmarks with corrections and additions, and was completely prepared for reprinting.

Indeed, scientific merits of Max Solomonovich did not go unnoticed, although, by and large, he deserved much more recognition. His first scientific award (apart from the gold medals for school and graduation from university) was a diploma of the A.L. Myasnikov in 1978.

In 1986 he earned G.F. Lang Prize. In 1981, by order of the Minister of Health, he was awarded the "Excellence in Healthcare" badge. In those same years, an attempt was made to introduce Max Solomonovich to the rank of corresponding member of the USSR Academy of Medical Sciences. His classmates V.I. Medvedev, D.I. Tzank, I.P. Ashmarin (then, a Corresponding Member of the Academy of Medical Sciences), A.P. Kolesov (then, a member of the Presidium of the Academy of Medical Sciences), prof. V.A. Almazov (then, a member of the Supreme Council) petitioned for M.S. Kushakovsky, but, unfortunately, his candidacy was not approved. No further attempts were made.

In 1993, after leaving the post of head of the Department of Cardiology, Max Solomonovich was elected an Honorary Member of the Academic Council of the Academy and he was awarded a diploma No. 6. In 1996, by decree of the President of Russia, prof. M.S. Kushakovsky was awarded the title of "Honored Worker of Science of the Russian Federation". In 2001, he was awarded the title of "Honorary Doctor" of the St. Petersburg Medical Academy of Postgraduate Education, as well as the title of "Honorary Cardiologist of Russia".

He also earned military awards: he was a holder of the Orders of the Red Star, the Patriotic War, the medals For Courage, For Military Merit, For Victory over Germany, and a number of others.

Max Solomonovich was loved and admired by the staff of the department, the hospital where he had worked for 35 years, his colleagues at the Academy, and medical students. His lectures, clinical discussions, rounds have always gathered a lot of doctors' attention. He was respected for his truly inexhaustible knowledge, constant benevolence and for being a true gentleman.

Professor Max Solomonovich Kushakovsky died suddenly on June 11, 2002. It happened unexpectedly for everyone, in the morning, when he, going to work, was waiting for a taxi

that had already been called. A world-famous scientist who created a large scientific school and glorified domestic science with innovative works in the field of therapy and cardiology has passed away. In 2003, the Department of Cardiology of St. Petersburg Medical Academy of Postgraduate Education was named after him. Since 2011, after the merger of St. Petersburg Medical Academy of Postgraduate Education and Leningrad Sanitary and Hygienic Medical Institute, the combined Department of Hospital Therapy and Cardiology has born his name.

Max Solomonovich Kushakovsky will always remain in the memory of friends, colleagues and grateful students who served the same goal together with him — the protection of people's health.

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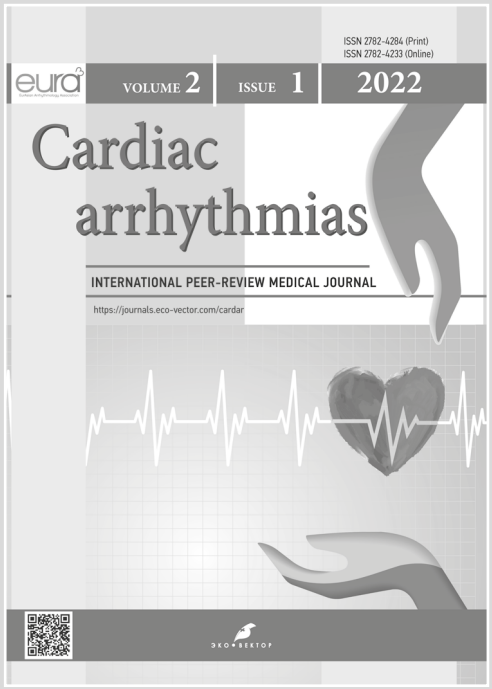
ЭКО • ВЕКТОР

CARDIAC ARRHYTHMIAS



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