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BALANCING BETWEEN CLINICAL EFFICACY AND ECONOMIC EXPEDIENCY: CHOOSING A DEVICE FOR CARDIAC RESYNCHRONIZATION THERAPY

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The article focuses on the analysis of device selection for cardiac resynchronization therapy based on the stratification of sudden cardiac death risk. Various diagnostic methods and clinical-anamnestic data are considered, along with their role in predicting arrhythmogenic events and making implantation decisions. Differences in implantation approaches for patients with ischemic and non-ischemic cardiomyopathy are discussed, emphasizing the importance of a combined risk assessment and the use of prognostic models. Unresolved issues related to optimal patient selection, timing for evaluating CRT effectiveness, and potential implantation strategies considering both economic and clinical factors are also reviewed.

Key words: chronic heart failure; ventricular tachyarrhythmias; sudden cardiac death; implantable cardioverter-defibrillator; cardiac resynchronization therapy

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According to epidemiological studies, chronic heart failure (CHF) affects 1-2% of the adult population in developed countries. In Russia, the prevalence of CHF has increased significantly in recent years: from 4.9% to 10.2% between 1998 and 2014. At the turn of the 21st century, in the European part of Russia, the prevalence of CHF of any New York Heart Association (NYHA) functional class was 7.0%, with severe forms of CHF (NYHA class III-IV) diagnosed in 2.1% of the population [1].

A particularly challenging category in terms of cardiovascular risk assessment and prediction of adverse events are patients with reduced left ventricular ejection fraction (LVEF). It has been demonstrated that when LVEF falls below 35%, such patients enter a high-risk group for sudden cardiac death (SCD) [2] and death due to acute decompensation of cardiac function, with SCD accounting for 15-20% of all fatal cases [3, 4].

SCD is primarily caused by the development of ventricular tachyarrhythmias (VT), which can be effectively terminated by implantable cardioverter-defibrillator (ICD) therapy. The device acts through antitachycardia pacing or shock delivery [5]. Therefore, ICD implantation is recommended for all patients with heart failure with reduced ejection fraction (HFrEF) who belong to the high-risk group for SCD, as well as for patients who have already survived an SCD episode or have had documented sustained VT. While the clinical rationale for ICD implantation as secondary prevention is beyond doubt in the professional community, the issue of selecting patients with HFrEF for interventional primary prevention of SCD increasingly becomes the subject of active discussion and debate [6].

It should be remembered that ICD implantation provides access to life-saving therapy but does not prevent the occurrence of arrhythmic events in the future. By contrast, another interventional treatment for CHF—cardiac resynchronisation therapy (CRT), indicated in HFrEF patients with a wide QRS complex on the electrocardiogram (ECG)—not only improves LV contractility [7], reduces the likelihood of repeated CHF hospitalisations [8], and enhances quality of life [9], but also has the potential to modify arrhythmic risk [10]. The principle of CRT is to correct atrioventricular and interventricular dyssynchrony by combining endocardial stimulation of the right ventricle with epicardial stimulation of the LV, synchronised with atrial systole. A positive response to CRT is considered a favourable prognostic marker [7]. Given that a responder to CRT may no longer meet the indications for ICD implantation, the question arises whether to implant a CRT-P (CRT with pacemaker function only) or a CRT-D (CRT with defibrillator function).

The problem of selecting the type of CRT device depending on the presence or absence of a defibrillator function is highly relevant due to the need to balance clinical efficacy, safety, economic feasibility, and individual patient characteristics. This underscores the demand for research in this field.

CRT - INDICATIONS AND RESPONSE PATTERNS TO THERAPY

The main indications for CRT are LVEF ≤35% and QRS duration ≥150 ms in the presence of left bundle branch block (LBBB) morphology. CRT is also indicated in patients with a wide QRS complex without LBBB morphology, although these indications carry a lower level of evidence [11]. In patients with HFrEF, interventricular and intraventricular conduction disturbances, including LBBB, are observed in approximately 30% of cases [12]. Current national and international guidelines recognise CRT as a highly effective treatment for such patients, as it has been shown to improve contractile function, reduce symptoms, enhance quality of life, and decrease both mortality and hospitalisation rates in patients with CHF [11].

It is well known that LBBB is an unfavourable marker that worsens prognosis in patients with CHF [12]. This is attributed to the development of interventricular dyssynchrony, in which right ventricular contraction occurs before left ventricular systole. The resulting interventricular and intraventricular dyssynchrony arises from the propagation of the electrical signal through the interventricular septum, leading to early activation of the septal region of the LV, while a zone of delayed activation appears in the posterior-basal wall of the LV. This mechanical mismatch causes presystolic stretching of the late-activated regions, which, in line with the Frank-Starling mechanism, augments systolic contraction. Consequently, systolic stress, tension, and myocardial oxygen consumption increase in the late-activated areas and decrease in the early-activated regions. The subsequent loss of contractile efficiency leads to the development of heart failure [13].

The response criteria for CRT described in the literature can be classified into several main categories:

- Clinical response - improvement in CHF functional class according to NYHA, improved quality of life.
- Echocardiographic (Echo) response - increase in LVEF, reduction in LV end-systolic volume (LVESV), reduction in mechanical dyssynchrony.
- Electrocardiographic response - narrowing of the QRS complex by ≥10 ms.

These response categories influence the achievement of various endpoints, including reduced hospitalisations, lower all-cause and cardiovascular mortality, and decreased arrhythmic risk [14].

As a clinical response criterion, improvement in CHF functional class according to NYHA is traditionally considered. In a study by Toshiko Nakai et al. [15], patients were assessed by both clinical and echocardiographic criteria. Those who showed improvement in NYHA class demonstrated better clinical outcomes after implantation, particularly regarding CHF-related hospitalisations and cardiovascular mortality.

The effect of electrocardiographic response was examined in a meta-analysis by George Bazoukis et al. [16], which found that narrowing of the QRS complex after CRT implantation was associated both with improvement in NYHA class and with a reduction in LVESV. QRS duration is undoubtedly a prognostic marker that increases the likelihood of response; however, QRS width on ECG is closely linked to LV volumetric parameters as measured by Echo. According to R.A. Stewart et al., each 10 ms increase in QRS duration was associated with an 8.3% increase in LV myocardial mass, a 9.2% increase in LV end-diastolic volume, and a 7.8% increase in LVESV [17]. In a study by N. Yamamoto et al., a modified QRS duration index—defined as the ratio of QRS duration to LV end-diastolic volume—significantly increased the probability of CRT response in patients with an "intermediate" QRS width (120-149 ms) on ECG [9].

The "gold standard" of a positive haemodynamic response is considered an increase in LVEF by ≥5% or a reduction in LVESV by ≥15%. These changes have a proven effect on all-cause mortality, arrhythmic risk, and cardiovascular mortality [14, 18].

It is important to emphasise that the effect of CRT is not limited to improving LV contractile function and CHF functional class. It also includes a reduction in myocardial electrical heterogeneity, which may contribute to lowering arrhythmic risk. For example, a decrease in LVESV and an increase in LVEF are associated not only with improved functional indices but also with a reduced likelihood of developing VT. In a study by N.N. Ilov et al., a reduction in LVESV by ≥15% and an increase in LVEF by ≥5% significantly decreased the risk of ventricular arrhythmias [4].

These results were corroborated in the PREDICT-CRT study, where haemodynamic response was associated with reduced all-cause mortality [18]. However, it should be noted that a direct correlation between changes in individual haemodynamic parameters and a reduction in VT risk is not always observed. For example, in a study by V.A. Kuznetsov et al. [19], which assessed the impact of response to CRT based on NYHA class, LVEF, and LVESV on overall mortality, concordance between response criteria was found to be low, and only the echocardiographic parameter (LVESV) demonstrated a moderate inverse correlation with mortality.

The impact of positive LVESV dynamics on cardiovascular mortality has been confirmed in further studies [18, 20]. Nevertheless, as shown by A. Van der Heijden et al., although the probability of VT decreased over a 5-year follow-up in patients with a "super-response" in LVESV, there were no statistically significant differences between responders and non-responders to CRT [20]. Similarly, M. Linhart et al., contrary to the above findings, did not demonstrate an effect of CRT on the occurrence of VT, noting that only the presence of myocardial scar was a significant predictor [21]. T. Nakamura et al. also reported no association between CRT response and VT occurrence [22].

These observations highlight that the efficacy of CRT in reducing life-threatening arrhythmias depends not only on the degree of improvement in contractile function but also on its impact on the electrical properties of the myocardium and the presence of substrate for VT.

In the absence of a haemodynamic response to CRT, a proarrhythmic effect may instead be observed, associated with progressive dispersion of repolarisation. This is supported by studies showing that lack of reverse remodelling was associated with increased VT incidence. M. Cvijić et al. [23] demonstrated that reverse remodelling reduces myocardial electrical heterogeneity, whereas in the ab-

sence of response to CRT, progressive repolarisation dispersion occurs. A published meta-analysis (8,000 patients) showed that the incidence of ventricular arrhythmias was 24% higher in patients with CRT non-response compared with those with implanted ICDs [24].

Thus, CRT demonstrates the ability to reduce SCD risk in the presence of a pronounced haemodynamic response and absence of substrate for VT, but requires close monitoring to prevent potential adverse effects in non-responders. A reduction in arrhythmic risk may therefore be regarded as a favourable effect of CRT response..

CRT-D OR CRT-P?

It seems logical to assume that in patients with a high probability of haemodynamic response to CRT, implantation of a device without a defibrillator function (CRT-P) would be reasonable, as this would help to avoid the well-known adverse events associated with ICDs and reduce treatment costs. However, this assumption is not always supported by clinical trial data.

For instance, results from the Swedish registry comparing patients with CRT-P and CRT-D demonstrated that those receiving CRT-D had lower 1- and 3-year all-cause and cardiovascular mortality [25]. The authors noted that patients who received CRT-P were older and had higher LVEF, which may have partly influenced the outcomes. Increased mortality in the CRT-P group was attributed to causes of death that an ICD would not have been able to prevent.

These findings are corroborated by the COMPANION trial, in which CRT-D reduced the risk of death by 24%. Similar results were observed in the REVERSE study, where CRT-D lowered 5-year mortality by 65% [26, 27]. A likely explanation for these results is the reduction in SCD in the CRT-D group. Nevertheless, a significant factor when interpreting these data is the aetiology of heart failure. For example, a subgroup analysis of the DANISH trial, which included patients with non-ischaemic HFrEF, showed that CRT-D did not reduce all-cause mortality [28].

Russian clinical guidelines do not yet provide specific recommendations for choosing between CRT-P and CRT-D. European guidelines suggest a somewhat broader approach, indicating that CRT-D should be more strongly considered in younger patients and in those with a likely proarrhythmic substrate, particularly when confirmed by gadolinium-enhanced cardiac MRI. However, they emphasise that clear criteria do not currently exist, and device selection should be individualised for each patient [29].

Thus, the decision regarding the choice of device for CRT remains complex and requires consideration of multiple factors, including patient age and preferences, the aetiology of heart failure, and the expected haemodynamic response to therapy. Importantly, the presence of a proarrhythmic substrate remains a decisive factor, as it significantly increases the likelihood of SCD.

SEARCH FOR THE SUBSTRATE OF VENTRICULAR TACHYCARDIA

The risk of SCD is determined by the presence of an anatomical substrate (myocardial hypertrophy, post-infarction cardiosclerosis, fibrosis) and electrophysiological changes (enhanced automaticity, triggered activity, dispersion of refractory periods) [9]. Identifying the potential substrate of VT remains a key task in SCD risk stratification.

Instrumental methods can provide additional information about the presence of a substrate and help decide on ICD implantation. Routine ECG diagnostics can be used to search for a potential substrate. On ECG analysis, dispersion of refractory periods can be assessed, manifested as QT interval prolongation/shortening [30] or changes in the interval from the T-wave peak to its end [31]. Other potential ECG markers of substrate include signs of early ventricular repolarisation [32] and LV hypertrophy [6]. It is noted that combining several markers significantly increases the prognostic value of ECG criteria, even in patients with LVEF >35% [33].

Transthoracic Echo, in addition to assessing LVEF, provides information on structural cardiac changes such as chamber volumes, wall thickness, LV mass, and regional wall motion abnormalities [34, 35]. Promising newer Echo techniques include tissue Doppler and two-dimensional strain imaging. Studies have shown that assessing longitudinal, radial, and circumferential myocardial strain, global longitudinal strain, and mechanical dispersion can improve diagnostic accuracy for VT substrate [36].

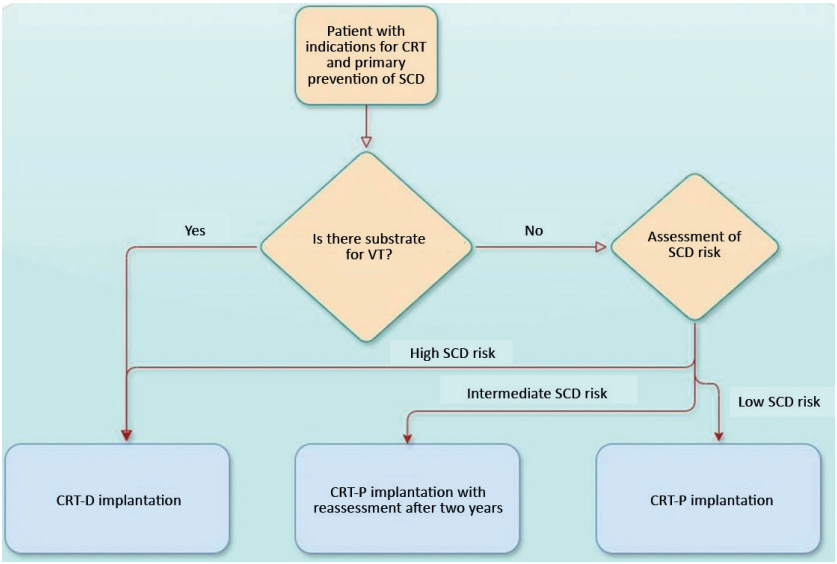

Fig. 1. Algorithm for device selection, where CRT - cardiac resynchronisation therapy; VT - ventricular tachycardia; SCD - sudden cardiac death.

Cardiac MRI with late gadolinium enhancement (LGE) occupies an important place in detecting potential VT substrate. Clinical guidelines recommend using this method as an additional factor when deciding on ICD implantation [37]. Gadolinium-based contrast accumulates in fibrotic tissue and visualises arrhythmogenic substrate [38]. Studies in patients with ischaemic cardiomyopathy (ICM) indicate that the presence of LGE zones is associated with increased risk of all-cause mortality and arrhythmic events [39]. A study

by colleagues in Penza confirmed the well-established link between LGE and SCD risk [40]. It is noted that when LGE exceeds 14% of LV myocardial mass, there is a direct correlation with ICD therapies.

Instrumental methods thus provide important information on anatomical and electrophysiological substrate, aiding ICD decision-making. Confirmed presence of a VT substrate should undoubtedly be a decisive factor for device implantation. However, these methods have limitations: they are not always absolutely precise, require substantial costs, and are not universally available. Therefore, it is important to consider not only diagnostic test results but also multiple other factors such as clinical data, history, and comorbidities [41].

The effectiveness of ICD use in patients with ICM is unquestionable. The predictive value of coronary artery disease for SCD is confirmed by a meta-analysis by Vikash Jaiswal et al., including data from 13 randomised studies [42]. Naturally, patients with ICM have high SCD risk due to the likely presence of VT substrate. Formation of arrhythmogenic substrate is related to peri-infarct zones surrounding scar tissue. These zones, containing partially viable cardiomyocytes, create electrical anisotropy, facilitating re-entry mediated VT [40, 43].

By contrast, the evidence base for ICD use in patients with non-ischaemic cardiomyopathy (NICM) is less convincing. Although the DANISH, DEFINITE, and SCD-HeFT trials demonstrated reduced SCD risk in ICD patients, they did not show a statistically significant effect on all-cause mortality [44-46]. This is attributed to the relatively lower proportion of SCD in overall mortality in these cohorts. It can reasonably be assumed that the substrate for VT in NICM is less extensive. Experimental data indicate that LV fibrosis in NICM patients significantly increases SCD risk [47]. Fibrotic zones with delayed conduction, increased automaticity, and myocardial refractory dispersion create conditions for VT. Thus, the presence of VT substrate appears to be the key factor for deriving maximum benefit from ICD implantation [48].

Experts agree that a single-factor approach is ineffective for this problem. Improved SCD risk stratification is possible only through a combined assessment method incorporating multiple predictors and the development of prognostic models.

Of particular interest is the use of prognostic scoring systems such as the MADIT-ICD Benefit Score, ESTIMATED Score, SCD-HeFT score analysis, and the Seattle Heart Failure Model [49-52]. These tools incorporate numerous factors to improve stratification of SCD risk and all-cause mortality in patients with HFrEF. Their analysis includes both predictors of VT substrate from available instrumental and laboratory studies, and clinical-anamnestic data [32]. Such models allow estimation of the benefit of ICD implantation by comparing SCD risk with all-cause mortality for an individual patient. The higher the probability of SCD, the greater the benefit of ICD therapy [49-51].

Particular attention should be paid to the MADIT-ICD Benefit Score, developed in 2020 from data from the largest MADIT trials (MADIT II, MADIT-CRT, MADIT-RIT, and MADIT-RISK). It is one of the most comprehensive prognostic models, created from a registry of over 4,500 patients. The calculator proposed by the authors incorporates predictors of VT and non-arrhythmic death. Predictors of VT include: male sex, age <75 years, heart rate (HR) >75 bpm, systolic blood pressure (SBP) <140 mmHg, LVEF ≤25%, and history of unstable VT, myocardial infarction, and atrial arrhythmias [49].

The calculator allows prediction of the likelihood of VT or non-arrhythmic death, assessing the potential benefit of ICD implantation. ROC analysis with external validation demonstrated high accuracy of the models: C-statistics of 0.75 for VT prediction and 0.67 for non-arrhythmic death. Within this context, the use of prognostic scales in patients with implanted CRT devices is of particular interest. As an independent factor influencing CRT outcomes, CRT itself was added to the MADIT-ICD Benefit Score and the Seattle Heart Failure Model, although separate analysis of CRT patients is available only from MADIT trial data [49, 52].

According to the MADIT-CRT analysis, treatment with CRT-D compared to ICD alone was associated only with a reduced risk of non-arrhythmic mortality [53]. A separate analysis excluding patients from MADIT-II showed similar results [49]. However, these studies also demonstrated that patients with QRS morphology consistent with LBBB experienced significant reduction in life-threatening arrhythmias, largely due to improved LV function and remodelling, confirming the positive effect of CRT on arrhythmic risk [54]. Yet, applying this model to assess ICD benefit in Russian patients yielded unsatisfactory results, underlining the need for local studies in this field [55].

UNRESOLVED PRACTICAL ISSUES AND PERSPECTIVES FOR THEIR RESOLUTION

It may be assumed that the presence of predictors of a positive response to CRT, an expected life expectancy of more than one year, and a low risk of SCD provide grounds for implanting a CRT-P device. However, despite the proven efficacy of CRT, according to various data, 30-40% of patients do not achieve the expected benefit from therapy [8, 56]. Factors reducing the likelihood of response to CRT include advanced CHF of high functional class, ICM with probable scarring in the pacing area, a baseline QRS complex that is insufficiently wide, or morphology not consistent with LBBB. Additional factors that may impair the probability of response include atrial fibrillation, chronic kidney disease, and baseline right ventricular dysfunction [57].

Equally important is determining the optimal follow-up period after implantation, after which the effects of CRT should be evaluated and further management decisions made to improve patient outcomes. In a study by T.V. Chumarnaya et al. [58], it was demonstrated that one year is sufficient in most cases to assess the clinical response, while reverse LV remodelling may continue for up to 24 months. Other studies also identify 12 months as adequate for CRT evaluation [59]. Based on these findings, a 24-month period after implantation reliably differentiates responders from non-responders, allowing subsequent treatment strategies to be defined.

An additional factor that could improve the efficacy of CRT-P is the use of conduction system pacing. In

this surgical approach, the lead is placed conventionally in the target vein of the coronary sinus to stimulate the LV, while another is implanted into the interventricular septum to capture the conduction system using the "stylet-driven" method, without dedicated delivery systems. The patients' response is assessed after two years. This strategy pursues two objectives: first, significantly increasing the probability of CRT response, as reflected in the LOT-CRT trial [60]; and second, if no response is observed after the maximum observation period, the option remains to implant a dual-chamber ICD with a DF-1 connector. In such cases, a shock lead is placed, while the previously implanted lead into the conduction system can be used for ventricular pacing, narrowing the QRS complex, potentially preventing CHF progression due to dyssynchrony, and avoiding LV pacing which, according to studies, increases the risk of VT in non-responders [24]. Possible limitations of this strategy include the risk of venous occlusion after initial implantation, the need for re-intervention in some non-responders after two years, and the technical skills required to place the lead into the conduction system.

Despite the large number of studies dedicated to predicting the probability of response to CRT, existing pre-implantation assessment algorithms remain imperfect, limiting their routine use in clinical practice. Nevertheless, the economic justification of CRT-P implantation as first-line therapy in patients with HFrEF is beyond doubt. CRT-P is more accessible in Russia due to its inclusion in the basic programme of mandatory health insurance. According to the Resolution of the Government of the Russian Federation of 27 December 2024, No. 1940 "On the Programme of State Guarantees of Free Medical Care to Citizens for 2025 and for the Planned Period of 2026 and 2027," reimbursement for CRT-P implantation amounts to 532,230 rubles, whereas CRT-D costs 1,281,144 rubles. This suggests a potential economic advantage from the more targeted use of CRT-D, reducing the number of such devices implanted under conditions of limited availability. An important clarification is that this strategy should be limited to patients with an indication for CRT and no evidence of VT substrate, confirmed by imaging modalities such as Echo, cardiac MRI with gadolinium, or invasive intracardiac electrophysiological study [3]. The algorithm for selecting between CRT-P and CRT-D is illustrated in Fig. 1. However, confirmation of this hypothesis requires further studies aimed at stratifying SCD risk in patients with indications for CRT.

CONCLUSION

The inclusion of funding for CRT device implantation in the basic programme of the Mandatory Health Insurance Fund has made CRT more accessible in our country, further emphasizing the relevance of the issue under discussion. It is likely that when selecting the optimal device for CRT, it is necessary to assess not only the baseline risk of SCD but also the probability of response to CRT and the potential for arrhythmic risk modification during therapy. The search for predictors and the development of prognostic systems aimed at evaluating such outcomes represent one of the priority tasks of contemporary cardiology, requiring prospective clinical studies that include domestic cohorts of patients with HFrEF.

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.). https://doi.org/10.18087/cardio.2021.4.n1628.

2. Vaduganathan M, Patel RB, Michel A, et al. Mode of Death in Heart Failure With Preserved Ejection Fraction. *J Am Coll Cardiol.* 2017;69: 556-69. https://doi.org/10.1016/j.jacc.2016.10.078.

3. Ilov NN, Palnikova OV, Stompel DR, et al. Risk stratification of sudden cardiac death in heart failure patients: is left ventricular ejection fraction alone sufficient? *Russian Journal of Cardiology.* 2021;26(1): 3959. (In Russ.). https://doi.org/10.15829/1560-4071-2021-3959.

4. Ilov NN, Palnikova OV, Stompel DR, et al. Clinical Predictors of Occurrence of Ventricular Tachyarrhythmias in Patients with Reduced Left Ventricle Ejection Fraction. Results of Single-Center Prospective Study. Kardiologiia. 2021;61(5): 32-40 (in Russ.). https://doi.org/10.18087/cardio.2021.5.n1480.

5. Revishvili ASh, Shlyahto EV, Popov SV, et al. Klinicheskie rekomendacii po primeneniyu kardioverterov-defibrillyatorov. In. Klinicheskie rekomendacii po provedeniyu elektrofiziologicheskih issledovanij, kateternoj ablyacii i primeneniyu implantiruemyh antiaritmicheskih ustrojstv. (Ed. Revishvili ASh, Shlyahto EV, Popov SV, et al.). Moscow 2017: 55-86 (in Russ.) ISBN 978-5-9500922-0-6.

6. Zaman S, Goldberger JJ, Kovoor P. Sudden Death Risk-Stratification in 2018-2019: The Old and the New. *Heart Lung Circ*. 2019;28: 57-64. https://doi.org/10.1016/j.hlc.2018.08.027.

7. Postol AS, Neminushchiy NM, Antipov GN, et al. Factors that Determined a Positive Response to Resynchronization Therapy in Patients With Chronic Heart Failure and Cardiac Dyssynchrony. One Center Experience. *Kardiologiia.* 2024;64(7): 31-39. (In Russ.) https://doi.org/10.18087/cardio.2024.7.n2627.

8. Glikson M, Israel C, Denmark C, et al. 2021 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy. *EHJ.* 2021: 1-94. https://doi.org/10.1093/eurheartj/ehab364.

9. Yamamoto N, Noda T, Nakano M, et al. Clinical utility of QRS duration normalized to left ventricular volume for predicting cardiac resynchronization therapy efficacy in patients with "mid-range" QRS duration. *Heart Rhythm*. 2024;21: 855-62. https://doi.org/10.1016/j.hrthm.2024.02.019.

10. Amara N, Boveda S, Defaye P, et al. Implantable cardioverter-defibrillator therapy among patients with non-ischaemic vs. ischaemic cardiomyopathy for primary prevention of sudden cardiac death. *Europace.* 2018;20: 65-72. https://doi.org/10.1093/europace/euw379.

11. Galyavich A.S., Tereshchenko S.N., Uskach T.M. et al. 2024 Clinical practice guidelines for Chronic heart failure. *Russian Journal of Cardiology.* 2024;29(11): 6162. (In Russ.). https://doi.org/10.15829/1560-4071-2024-6162.

12. Wallentin L, Stenestrand U, Tabrizi F, et al. Influence of left bundle branch block on long-term mortality in a population with heart failure. *EHJ.* 2007:2449-55. https://doi.org/10.1093/eurheartj/ehm262.
13. Moustafa AT, Tang ASL, Khan HR. Conduction system pacing on track to replace CRT ? Review of conduction system pacing. *Front Cardiovasc Med.* 2023: 1-12. https://doi.org/10.3389/fcvm.2023.1220709.
14. Ilov NN, Stompel DR, Palnikova OV, et al. 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.). https://doi.org/10.17116/kardio20221501119
15. Nakai T, Ikeya Y, Kogawa R, et al. What Are the Expectations for Cardiac Resynchronization Therapy ? A Validation of Two Response Definitions. *Journal of clinical medicine* 2021;10(3): 514. https://doi:10.3390/jcm10030514.
16. Bazoukis G, Naka KK, Alsheikh-Ali A, et al. Association of QRS narrowing with response to cardiac resynchronization therapy - a systematic review and meta-analysis of observational studies. *Heart Failure Reviews* 2020;25: 745-56. https://doi.org/10.1007/s10741-019-09839-5.
17. Stewart RA, Young AA, Anderson C et al. Relationship between QRS duration and left ventricular mass and volume in patients at high cardiovascular risk. *Heart* 2011;97: 1766-70. https://doi.org/10.1136/heartjnl-2011-300297.
18. Stankovic I, Belmans A, Prinz C, et al. The association of volumetric response and long-term survival after cardiac resynchronization therapy *European Heart Journal - Cardiovascular Imaging.* 2017;18(10): 1109-17. https://doi.org/10.1093/ehjci/jex188.
19. Kuznetsov V.A., Soldatova A.M., Enina T.N. et al. Does the lack of left ventricular reverse remodeling always mean non - response to cardiac resynchronization therapy? *Terapevticheskii arkhiv.* 2019;91: 10-5 (in Russ.). https://doi.org/10.26442/00403660.2019.12.000102.
20. van der Heijden AC, Höke U, Thijssen J, et al. Super-responders to cardiac resynchronization therapy remain at risk for ventricular arrhythmias and benefit from defibrillator treatment. *European Journal of Heart Failure*. 2014;16: 1104-11. https://doi.org/10.1002/ejhf.152.
21. Linhart M, Doltra A, Acosta J, et al. Ventricular arrhythmia risk is associated with myocardial scar but not with response to cardiac resynchronization therapy. *EP Europace.* 2020;22: 1391-400. https://doi.org/10.1093/europace/euaa142.
22. Nakamura T, Fukuzawa K, Kiuchi K et al. Ventricular arrhythmia events in heart failure patients with cardiac resynchronization therapy with or without a defibrillator for primary prevention. *J Arrhythmia*. 2022;38: 1056-62. https://doi.org/10.1002/joa3.12795.
23. Cvijić M, Antolič B, Klemen L, et al. Repolarization heterogeneity in patients with cardiac resynchronization therapy and its relation to ventricular tachyarrhythmias. *Heart Rhythm.* 2018;15: 1784-90. https://doi.org/10.1016/j.hrthm.2018.06.023.
24. Deif B, Ballantyne B, Almehmadi F, et al. Cardiac resynchronization is pro-arrhythmic in the absence of reverse ventricular remodelling: a systematic review and meta-analysis. *Cardiovascular Research*. 2018;114(11): 1435-44. https://doi.org/10.1093/cvr/cvy182.
25. Schrage B, Lund LH, Melin M, et al. Cardiac resynchronization therapy with or without defibrillator in patients with heart failure. *EP Europace*. 2022;24: 48-57. https://doi.org/10.1093/europace/euab233.
26. Bristow MR, Saxon LA, Boehmer J, et al. Cardiac-resynchronization therapy with or without an implantable defibrillator in advanced chronic heart failure. *The New England journal of medicine.* 2004;350(21): 2140-50. https://doi.org/10.1056/NEJMoa032423.
27. Linde C, Abraham WT, Gold MR et al. Randomized Trial of Cardiac Resynchronization in Mildly Symptomatic Heart Failure Patients and in Asymptomatic Patients With Left Ventricular Dysfunction and Previous Heart Failure Symptoms. *JACC.* 2008;52(23): 1834-43. https://doi.org/10.1016/j.jacc.2008.08.027.
28. Kober L, Thune JJ, Nielsen JC et al. Defibrillator implantation in patients with nonischemic systolic heart failure. *The New England journal of medicine*. 2016;375: 1221-30. https://doi.org/10.1056/NEJMoa1608029.
29. Glikson M, Nielsen JC, Kronborg MB, et al. 2021 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy: Developed by the Task Force on cardiac pacing and cardiac resynchronization therapy of the European Society of Cardiology (ESC) With the special contribution of the European Heart Rhythm Association (EHRA). *European Heart Journal.* 2021;42: 3427-520. https://doi.org/10.1093/eurheartj/ehab364.
30. Ramalho D, Freitas J. Drug-induced life-threatening arrhythmias and sudden cardiac death: A clinical perspective of long QT, short QT and Brugada syndromes. *Revista Portuguesa de Cardiologia.* 2018;37: 435-46. https://doi.org/10.1016/j.repc.2017.07.010.
31. Tse G, Gong M, Wong WT, et al. The T(peak) - T(end) interval as an electrocardiographic risk marker of arrhythmic and mortality outcomes: A systematic review and meta-analysis. *Heart Rhythm.* 2017;14: 1131-7. https://doi.org/10.1016/j.hrthm.2017.05.031.
32. Pranata R, Yonas E, Vania R, et al. Electrocardiographic early repolarization is associated with future ventricular arrhythmia after acute myocardial infarction-Systematic Review and Meta-Analysis. *Journal of Arrhythmia.* 2019;35: 626-35. https://doi.org/10.1002/joa3.12196.
33. Aro AL, Reinier K, Rusinaru C, et al. Electrical risk score beyond the left ventricular ejection fraction: prediction of sudden cardiac death in the Oregon Sudden Unexpected Death Study and the Atherosclerosis Risk in Communities Study. *European Heart Journal.* 2017;38: 3017-25. https://doi.org/10.1093/eurheartj/ehx331.
34. van der Bijl P, Delgado V, Bax JJ. Imaging for sudden cardiac death risk stratification: Current perspective and future directions. *Progress in cardiovascular diseases.* 2019;62: 205-11. https://doi.org/10.1016/j.pcad.2019.04.005.
35. Chatterjee S, Bavishi C, Sardar P et al. Meta-analysis of left ventricular hypertrophy and sustained arrhythmias. *American Journal of Cardiology.* 2014;114: 1049-52. https://doi.org/10.1016/j.amjcard.2014.07.015.
36. Golukhova E.Z., Bulaeva N.I., Mrikaev D.V. et al. Prognostic value of left ventricular global longitudinal strain and mechanical dispersion by speckle tracking echocardiography

in patients with ischemic and nonischemic cardiomyopathy: a systematic review and meta-analysis. *Russian Journal of Cardiology*. 2022;27(3S): 5034 (in Russ.). https://doi.org/10.15829/1560-4071-2022-5034.
37. Zeppenfeld K, Tfelt-Hansen J, de Riva M, et al. 2022 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death. *European Heart Journal.* 2022;43: 3997-4126. https://doi.org/10.1093/eurheartj/ehac262.
38. Golukhova EZ, Aleksandrova SA, Berdibekov BS. Predictive role of quantification of myocardial fibrosis using delayed contrast-enhanced magnetic resonance imaging in nonischemic dilated cardiomyopathies: a systematic review and meta-analysis. *Russian Journal of Cardiology.* 2021;26: 189-97 (in Russ.). https://doi.org/10.15829/1560-4071-2021-4776.
39. Shlevkov NB, Zhambeev AA, Gasparyan AZ, et al. Characteristic of fibrotic myocardial lesions associated with life-threatening ventricular tachyarrhythmias in patients with ischemic and non-ischemic cardiomyopathies. *Terapevticheskii arkhiv.* 2018;90(9): 42-7 (in Russ.). https://doi.org/10.26442/terarkh201890942-47.
40. Bazylev V.V., Ushakov R.Yu., Durmanov S.S. et al. Prognostic value of delayed gadolinium enhancement on cardiac magnetic resonance imaging in patients with ischemic cardiomyopathy and an implanted cardioverter-defibrillator. *Journal of Arrhythmology*. 2024;31(2): 35-43 (in Russ.)]. https://doi.org/10.35336/VA-1260.
41. Narins CR, Aktas MK, Chen AY, et al. Arrhythmic and Mortality Outcomes Among Ischemic Versus Nonischemic Cardiomyopathy Patients Receiving Primary ICD Therapy. *JACC Clinical Electrophysiology.* 2022;8: 1-11. https://doi.org/10.1016/j.jacep.2021.06.020.
42. Jaiswal V, Taha AM, Joshi A, et al. Implantable cardioverter defibrillators for primary prevention in patients with ischemic and non-ischemic cardiomyopathy: A meta-analysis. *Current Problems in Cardiology.* 2024;49: 102198. https://doi.org/10.1016/j.cpcardiol.2023.102198.
43. Burke AP, Virmani R. Pathophysiology of acute myocardial infarction. *Medical Clinics of North America*. 2007;91(4): 553-72; ix. https://doi.org/10.1016/j.mcna.2007.03.005.
44. Køber L, Thune JJ, Nielsen JC, et al. Defibrillator Implantation in Patients with Nonischemic Systolic Heart Failure. *The New England Journal of Medicine*. 2016;375: 1221-30. https://doi.org/10.1056/NEJMoa1608029.
45. Kadish A, Dyer A, Daubert JP et al. Prophylactic Defibrillator Implantation in Patients with Nonischemic Dilated Cardiomyopathy. *The New England Journal of Medicine*. 2004;350: 2151-8. https://doi.org/10.1056/NEJMoa033088.
46. Moss AJ, Zareba W, Hall WJ, et al. Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction. *The New England Journal of Medicine*. 2002;346: 877-83. https://doi.org/10.1056/NEJMoa013474.
47. Gulati A, Jabbour A, Ismail TF, et al. Association of fibrosis with mortality and sudden cardiac death in patients with nonischemic dilated cardiomyopathy. *JAMA* 2013;309: 896-908. https://doi.org/10.1001/jama.2013.1363.
48. Gold MR, Daubert J-C, Abraham WT, et al. Implantable Defibrillators Improve Survival in Patients With Mildly Symptomatic Heart Failure Receiving Cardiac Resynchronization Therapy. *Circulation Arrhythmia and Electrophysiology.* 2013;6: 1163-8. https://doi.org/10.1161/CIRCEP.113.000570.
49. Younis A, Goldberger JJ, Kutyifa V, et al. Predicted benefit of an implantable cardioverter-defibrillator: the MADIT-ICD benefit score. *European Heart Journal* 2021;42: 1676-84. https://doi.org/10.1093/eurheartj/ehaa1057.
50. Li X, Fan X, Li S, et al. A Novel Risk Stratification Score for Sudden Cardiac Death Prediction in Middle-Aged, Nonischemic Dilated Cardiomyopathy Patients: The ESTIMATED Score. *Canadian Journal of Cardiology.* 2020;36: 1121-9. https://doi.org/10.1016/j.cjca.2019.11.009.
51. Reeder HT, Shen C, Buxton AE, et al. Joint Shock/Death Risk Prediction Model for Patients Considering Implantable Cardioverter-Defibrillators. *Circulation Cardiovascular Quality and Outcomes*. 2019;12: e005675. https://doi.org/10.1161/CIRCOUTCOMES.119.005675.
52. Mozaffarian D, Anker SD, Anand I, et al. Prediction of mode of death in heart failure: the Seattle Heart Failure Model. *Circulation*. 2007;116: 392-8. https://doi.org/10.1161/CIRCULATIONAHA.106.687103.
53. Moss AJ, Hall WJ, Cannom DS, et al. Cardiac-resynchronization therapy for the prevention of heart-failure events. *The New England Journal of Medicine.* 2009;361: 1329-38. https://doi.org/10.1056/NEJMoa0906431.
54. Goldenberg I, Aktas MK, Zareba W, et al. QRS Morphology and the Risk of Ventricular Tachyarrhythmia in Cardiac Resynchronization Therapy Recipients. *JACC Clinical Electrophysiology.* 2024;10: 16-26. https://doi.org/10.1016/j.jacep.2023.09.018.
55. Ilov NN, Boytsov SA, Nechepurenko A.A. Whether to implant a defibrillator or not? The Possibility of Using the MADIT-ICD Benefit Score Calculator in Real Practice. *Kardiologiia.* 2024;64(2): 27-33. (in Russ.). https://doi.org/10.18087/cardio.2024.2.n2447.
56. Mei DA, Gerra L, Imberti JF, et al. Cardiac resynchronization therapy (CRT) nonresponders in the contemporary era : A state-of-the-art review. *Heart Rhythm*. 2024: 1-11. https://doi.org/10.1016/j.hrthm.2024.05.057.
57. Cleland J, Freemantle N, Ghio S, et al. Predicting the Long-Term Effects of Cardiac Resynchronization Therapy on Mortality From Baseline Variables and the Early Response. *JACC*. 2008;52. https://doi.org/10.1016/j.jacc.2008.04.036.
58. Chumarnaya TV, Lyubimtseva TA, Solodushkin SI et al. Evaluation of the long-term effectiveness of cardiac resynchronization therapy. *Russian Journal of Cardiology*. 2021;26(7): 4531 (in Russ.). https://doi.org/10.15829/1560-4071-2021-4531.
59. Szabó KM, Tóth A, Nagy L, et al. Add-on Sacubitril/Valsartan Therapy Induces Left Ventricular Remodeling in Non-responders to Cardiac Resynchronization Therapy to a Similar Extent as in Heart Failure Patients Without Resynchronization. *Cardiology and Therapy.* 2024;13: 149-61. https://doi.org/10.1007/s40119-023-00346-1.
60. Jastrzębski M, Moskal P, Huybrechts W, et al. Left bundle branch-optimized cardiac resynchronization therapy (LOT-CRT): Results from an international LBBAP collaborative study group. *Heart Rhythm*. 2022;19: 13-21.

https://doi.org/10.1016/j.hrthm.2021.07.057.
61. Strauss DG. Differentiation between left bundle branch block and left ventricular hypertrophy: Implications for cardiac resynchronization therapy. *Journal of Electrocardiology.* 2012;45: 635-9. https://doi.org/10.1016/j.jelectrocard.2012.09.001.