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CARDIAC RESYNCHRONIZATION THERAPY: TOWARDS PERSONALIZED DEVICE SELECTION. RESULTS OF A TWO-YEAR PROSPECTIVE STUDY

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Aim. To conduct a comparative analysis of clinical, instrumental, and laboratory diagnostic methods and to identify factors determining the likelihood of sustained paroxysmal ventricular tachyarrhythmias (VT) in patients with indications for cardiac resynchronization therapy (CRT).

Methods. The study included 124 patients with chronic heart failure (CHF) and an implanted CRT-D system. The median age was 58 (52-63) years. Patients were followed for 24 months. Clinical and demographic characteristics, electrocardiographic data, speckle-tracking echocardiographic parameters, and blood biomarker levels were assessed. The primary endpoint was the occurrence of sustained VT episodes recorded by the implanted device. A multivariate logistic regression model was developed to predict the two-year probability of VT occurrence.

Results. During the follow-up period, 29 patients (23.3%) experienced episodes of sustained VT. Univariate analysis identified seven candidate predictors with the highest potential for reaching the endpoint. These included: clinical factors (presence of coronary artery disease and atrial fibrillation); ECG parameters (modified QRS index >0.6, presence of left bundle branch block (LBBB) according to Strauss criteria); echocardiographic findings (global longitudinal strain ≥ -6%, mitral regurgitation of grade 2 or higher); and laboratory markers (galectin-3 ≥ 12 ng/mL). Based on these variables, a predictive model was developed using binary logistic regression to estimate the two-year risk of VT in patients with CRT indications. The Strauss LBBB criterion, although statistically significant in univariate analysis, was not included in the final model. At a regression function cut-off value of 0.228, the model demonstrated a diagnostic accuracy of 73.6% (sensitivity - 86.2%, specificity - 69.6%). The area under the ROC curve was 0.779, which, according to expert grading, indicates good model performance.

Conclusion. The study identified several independent predictors of sudden cardiac death risk in patients with implanted CRT-D devices and enabled the construction of a multifactorial prognostic model. The findings suggest the potential for developing a personalized algorithm for device selection.

Key words: chronic heart failure; cardiac resynchronization therapy; ventricular tachyarrhythmias; risk stratification

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Despite significant advances in pharmacological therapy and implantable device technologies, chronic heart failure (CHF) remains one of the leading causes of mortality worldwide [1]. One of the most effective treatment strategies for patients with CHF, reduced left ventricular ejection fraction (LVEF), and signs of electrical dyssynchrony is cardiac resynchronisation therapy (CRT). CRT improves ventricular contraction synchrony, promotes reverse myocardial remodelling, alleviates symptoms, and increases survival rates [2, 3].

Currently, two types of devices are used in clinical practice to deliver CRT: CRT-P (CRT pacemaker without defibrillation function); CRT-D (CRT defibrillator with additional antiarrhythmic capabilities).

CRT-D devices also provide protection against sudden cardiac death (SCD) by delivering high-energy defibrillation or anti-tachycardia pacing (ATP) in the event of life-threatening ventricular tachyarrhythmias (VT) [4].

Although CRT-D appears to offer clear advantages in SCD prevention, the choice between CRT-P and CRT-D remains the subject of ongoing clinical and ethical debate. This is due to concerns regarding: increased risk of infectious complications [5], inappropriate shocks or unneces-

sary electrical therapy, the need for more frequent generator replacements in CRT-D patients [5, 6].

According to the Russian clinical guidelines for the management of CHF, the decision to implant either device type should be based not only on the risk of arrhythmic events and the presence of VT substrate but also on: the individual patient's clinical profile, prognosis and expected survival, quality of life, economic and social factors [7].

However, a specific algorithm for device selection is not provided. In the Russian Federation, CRT-P implantation can be performed at any medical facility operating under the national compulsory health insurance system, making this form of care more accessible to the population.

Large clinical trials such as COMPANION, MADIT-CRT, and others have demonstrated the overall efficacy of CRT. Nevertheless, evidence comparing the relative benefits of CRT-P versus CRT-D in specific patient subgroups remains inconsistent [8, 9]. Moreover, the patient's clinical profile may change over time, underscoring the

Table 1.

Clinical and Demographic Characteristics of Patients

	All patients (n=124)	Patients with VT (n=29)	Patients without VT (n=95)	p
Age, years	58 (52-63)	58 (50.5-63.5)	58 (53-63)	0.820
Male sex, n (%)	94 (76)	23 (79.3)	71 (74.7)	0.615
Body mass index, kg/m^2	29.7 (25.6-32.4)	29.1 (24.1-32.8)	29.8 (26-32.4)	0.508
Coronary artery disease, n (%)	44 (35.4)	14 (48.2)	30 (31.5)	0.1
Post-infarction cardiosclerosis, n (%)	26 (20.9)	9 (31)	17 (17.9)	0.128
Coronary artery lesions, n (%)	67 (54)	15 (51.7)	52 (54.7)	0.776
Arterial hypertension, n (%)	69 (55.6)	18 (62)	51 (53.6)	0.426
Diabetes mellitus, n (%)	27 (21.7)	7 (24.1)	20 (21)	0.725
Obesity, n (%)	55 (44.3)	12(41.3)	43(45.2)	
Stroke history, n (%)	5 (4)	1(3.4)	4(4.2)	0.855
Chronic kidney disease, n (%)	49 (40.8)	13(46.4)	36 (39.1)	0.491
Atrial fibrillation (any form), n (%)	40 (32.2)	15(51.7)	25 (26.3)	0.01
AF (paroxysmal/persistent), n (%)	31 (25)	10 (34.5)	21 (22.1)	0.178
AF (permanent), n (%)	9 (7.3)	5 (17.2)	4 (4.2)	0.018
History of non-sustained VT, n (%)	21 (16.9)	6 (20.7)	15 (15.7)	0.538
NT-proBNP, pg/mL	2268 (1204-4805)	2100 (1064-4177)	2476 (1267-5537)	0.347
sST2, ng/mL	27.1 (17.2-54.8)	39.2 (21.4-64.5)	26.8 (16.4-45.1)	0.154
CKD-EPI, mL/min/1.73 m^2	68 (60.2-77.4)	71.15 (63.8-88.5)	67.2 (59.5-76)	0.247
Cardiac surgery history				
Myocardial revascularisation, n (%)	35 (28.4)	11 (39.2)	24 (25.2)	0.148
Valve repair surgery, n (%)	16 (13)	5 (17.8)	11 (11.5)	0.385
Left ventricular reconstruction, n (%	1 (0.8)	0	1 (1)	0.586
Echocardiographic parameters				
LV EDV, mL	249 (204-304)	240 (211-294)	257 (203-307)	0.913
LV ESV, mL	177 (140-214)	170 (145.5-207)	188 (139-215.5)	0.694
LV EDD, cm	6.9 (6.35-7.5)	6.9 (6.4-7.35)	6.85 (6.3-7.6)	0.974
LV ESD, cm	5.8 (5.35-6.5)	5.6 (5.3-6.3)	5.8 (5.3-6.6)	0.265
LV ejection fraction (Simpson), %	29 (24-33)	30 (26.5-35)	29 (22-33)	0.099
GLS, %	6.9 (8.4-5.2)	5.1 (3.4-6.7)	7.5(5.4-8.5)	0.092
Electrocardiographic predictors				
QRS duration, ms	164 (150-180)	150 (120-175)	170 (152-190)	0.007
LBBB (Strauss criteria), n (%)	77 (63.6)	14 (48.2)	63 (68.4)	0.049
Modified QRS index	0.63 (0.53-0.79)	0.56 (0.49-0.74)	0.65 (0.54-0.79)	0.101

Note here and after: AF - atrial fibrillation; VT - ventricular tachycardia; NT-proBNP - N-terminal pro-brain natriuretic peptide; sST2 - soluble suppression of tumorigenesis-2; CKD-EPI - Chronic Kidney Disease Epidemiology Collaboration formula; LV - left ventricle; EDV - end-diastolic volume; ESV - end-systolic volume; EDD - end-diastolic diameter; ESD - end-systolic diameter; GLS - global longitudinal strain; LBBB - left bundle branch block.

need for a dynamic approach to device selection based on predictors of VT development.

It is evident that the risk of SCD is highest in patients with a verified VT substrate. Cardiac magnetic resonance imaging (MRI) with late gadolinium enhancement is a validated tool for visualising arrhythmogenic substrate with good sensitivity, as confirmed by multiple studies [10], and is also recommended as a decision-making factor in favour of ICD implantation [11]. However, due to its complexity and potential for false negatives, its widespread application is limited.

Thus, the device selection algorithm for CRT should be based on simpler, reproducible clinical, instrumental, and laboratory methods that are accessible in routine practice.

Aim: To conduct a comparative analysis of clinical, instrumental, and laboratory diagnostic methods, and to identify factors associated with the occurrence of sustained ventricular tachycardia (VT) episodes in patients eligible for CRT.

METHODS

The study design complied with international Good Clinical Practice (GCP) standards and the core principles of the Declaration of Helsinki. The study protocol was approved by the local ethics committee. All participants provided written informed consent prior to inclusion.

All patients underwent standard clinical evaluations as part of the diagnostic algorithm for CHF. In addition, speckle-tracking echocardiography was performed, along with the assessment of blood biomarkers, including: serum electrolytes, C-reactive protein, creatinine, soluble suppression of tumorigenicity-2 (sST2), N-terminal pro-brain natriuretic peptide (NT-proBNP), and galectin-3.

A total of 124 patients were included in the postoperative follow-up programme.Summary clinical and demographic characteristics of the patients are presented in Table 1.

Device Implantation and Subsequent Programming

Device implantation was performed in accordance with established clinical standards. A bipolar or quadripolar left ventricular lead was placed in the coronary sinus using a specialised delivery system. The lateral vein branch, anatomically located over the region of latest left ventricular activation in patients with complete left bundle branch block (CLBBB), was considered the preferred site for lead placement.

Device programming was carried out in three stages: intraoperatively, on postoperative days 4-5, and again three months after the procedure. Subsequent follow-up visits were scheduled once per year.

Pacing vector selection was guided by the lowest stimulation threshold and the absence of phrenic nerve capture. The atrioventricular delay was adjusted to achieve the highest possible percentage of biventricular pacing. Optimal interventricular delay was determined based on analysis of the duration of the paced ventricular QRS complex on ECG. Preference was given to the use of manufacturer-provided automatic optimisation algorithms.

To detect ventricular arrhythmias - the study's primary endpoint - a dual-zone detection scheme was employed: the VT zone was programmed to start at 160 bpm, and the ventricular fibrillation (VF) zone at 200 bpm. Supraventricular tachyarrhythmia discrimination algorithms were activated. Programming was aimed at minimising inappropriate therapies and prioritising ATP over high-energy shocks.

All study participants were followed for a period of 24 months. Follow-up visits were scheduled at 3, 12, and 24 months post-implantation. During these visits, recorded device-detected events were reviewed, including detection zone, episode date, accuracy of rhythm discrimination algorithms, and appropriateness of delivered therapy (ATP or shock).

Study Endpoint

The primary endpoint was defined as the first documented episode of sustained VTlasting ≥30 seconds and detected within the programmed VT monitoring zone, or any episode of VT or VFthat triggered delivery of electrical therapy, either ATP or shock.

Statistical Analysis

Statistical analysis was performed using both parametric and non-parametric methods. Initial data processing

Table 2.

Electrocardiographic Predictors of Ventricular Tachycardia (VT)

	All patients (n=124)	Patients with VT (n=29)	Patients without VT (n=95)	P
Sinus rhythm, n (%)	105 (85.4)	23 (79.3)	82 (87.2)	0.291
Atrial fibrillation, n (%)	40 (32.3)	15 (51.7)	25 (26.3)	0.01
LBBB#, n (%)	77 (63.6)	14 (48.2)	63 (68.4)	0.049
LBBB$, n (%)	49 (59)	12 (66.7)	37 (56.9)	0.457
SLI, n (%)	22 (22%)	6 (23.1)	16 (21.6)	0.878
CVI, n (%)	75 (75)	18 (69.2)	57 (77)	0.43
P wave, ms	120 (101-120)	110 (101-122)	120 (101-120)	0.802
P wave >120 ms, n (%)	25 (23.4)	6 (26.1)	19 (22.6)	0.728
QRS complex, ms	164 (150-180)	150 (120-175)	170 (152-190)	0.674
QTc interval, ms	492 (455-507)	482 (447-498)	492 (462-507)	0.216
Tp-Te interval, ms	100 (90-120)	100 (80-120)	100 (100-100)	0.743
Frontal QRS axis, °	156 (120-174)	156 (97-187)	157 (123-173)	0.855
QRSm	0.64 (0.53-0.80)	0.56 (0.49-0.74)	0.65 (0.54-0.80)	0.101
QRSm > 0,6, n (%)	77 (62.3)	13 (44.8)	64 (68.1)	0.024

Note: # - according to Strauss; $ - according to Surawizc; SLI - Sokolow-Lyon Index (Sv1 +Rv5 ≥35 мм, Rv5,v6 >26 мм); CVI - Cornell Voltage Index Sv_3 + RaVL > 28 mm for men, > 20 mm for women; QRSm - Modified QRS Index, ratio of QRS duration to the left ventricular end-diastolic volume (QRS duration / LVEDV)

and cleaning were carried out in Microsoft Excel 2010, while the statistical analyses were conducted using IBM SPSS Statistics version 23.

For continuous variables, the normality of distribution was assessed using the Kolmogorov-Smirnov test. If the data followed a normal distribution, results were presented as mean (M) ± standard deviation (SD), and comparisons between groups were made using Student's t-test. In cases where normality was not confirmed, data were reported as median (Me) and interquartile range (Q1-Q3), and group comparisons were performed using the Mann-Whitney U test.

For categorical variables, the Pearson χ^2 test was used. When analysing relative risks, odds ratios (ORs) were calculated. Statistical significance was considered achieved if the confidence interval excluded the null value (OR = 1). The significance level was set at $p < 0.05$.

To predict the 2-year risk of VT, a multivariate logistic regression model was developed. Missing data were imputed using median substitution from neighbouring points. Independent predictors were selected through stepwise backward elimination based on the Wald criterion. Model significance was evaluated using the χ^2 test, and the proportion of explained variance was assessed using Nagelkerke's R^2.

The model's predictive performance and threshold values were assessed using receiver operating characteristic (ROC) analysis, with calculation of the area under the curve (AUC). To facilitate application of the model in clinical settings, continuous variables included in the final model were transformed into nominal variables by identifying optimal cut-off values based on maximum sensitivity and specificity derived from the ROC curve.

RESULTS

A total of 124 patients with implanted CRT-D systems were included in the study. The mean LVEF was 29% (interquartile range: 24-33%). The mean age of participants was 58 years (IQR: 52-63), and the majority were male - 94 patients (76%). Prior to enrolment, 35 patients (28.4%) had undergone complete myocardial revascularisation, and 16 patients (13%)had received surgical correction of valvular pathology. All patients were receiving optimal guideline-directed medical therapy (GDMT) for chronic heart failure in accordance with the clinical recommendations valid at the time of study inclusion.

Table 3.

Multivariate Analysis of Echocardiographic Parameters

	All patients (n=124)	With VT (n=29)	Without VT (n=95)	P
LVEF (Simpson), %	29 (24-33)	30 (26,5-35)	29 (22-33)	0,095
GLS, %	7,3 (8,95-5,4)	4,6 (5,9-3,4)	7,6 (9,2-5,6)	0,014
LV EDV, mL	249,5 (204,5-304)	240 (212-290)	257 (203-305,5)	0,913
Indexed LV EDV, mL/m^2	126 (104-154)	125 (115-157,1)	127,1 (104-152,1)	0,664
LV ESV, mL	177 (140-214)	170 (147-205)	188 (140-214)	0,694
Indexed LV ESV, mL/m^2	90,1 (73,2-107,3)	82,7 (74-108,6)	90,4 (73,2-106)	0,890
LV EDD, cm	6,9 (6,35-7,5)	6,9 (6,4-7,3)	6,85 (6,3-7,6)	0,974
Indexed LV EDD, cm/m^2	3,5 (3,1-3,9)	3,5 (3,2-3,9)	3,5 (3-3,9)	0,575
LV ESD, cm	5,8 (5,35-6,55)	5,6 (5,5-6,3)	5,8 (5,35-6,6)	0,259
Indexed LV ESD, cm/m^2	2,9 (2,6-3,4)	2,8 (2,6-3)	3 (2,6-3,5)	0,020
IV septal thickness, cm	1 (0,85-1,1)	1 (0,9-1,2)	1 (0,8-1,1)	0,826
Posterior wall thickness, cm	1 (1-1,2)	1,1 (1-1,2)	1 (0,9-1,1)	0,045
Mean posterior wall thickness, cm	1 (0,9-1,1)	1,05 (0,95-1,15)	1 (0,9-1,1)	0,296
LV myocardial mass, g	311,7 (270,9-377,3)	292,9 (246,7-376,8)	311,7 (275,2-386,9)	0,523
sPAP, mmHg	43 (30-50)	30 (26-50)	44 (36-50)	0,014
LA sup-inf diameter, cm	6 (5,4-6,45)	6,1 (5,3-6,3)	6 (5,45-6,5)	0,314
LA medio-lateral diameter, cm	4,7 (4,3-5,1)	4,7 (4,3-5,2)	4,5 (4,2-4,7)	0,037
LA anteroposterior diameter, cm	4,6 (4,28-5)	4,6 (4,1-4,9)	4,6 (4,35-5,1)	0,277
Indexed LA volume, mL/m^2	95 (76,5-118)	98 (78-125)	86 (71,5-99)	0,030
RA sup-inf diameter, cm	5,3 (4,7-6)	4,95 (4,5-5,8)	5,4 (4,7-6)	0,107
RA medio-lateral diameter, cm	4 (3,5-4,6)	4,1 (3,7-4,6)	3,55 (3,3-4,35)	0,017
ARpat, n (%)	53 (47,3)	11 (42,3)	42 (48,8)	0,559
MRpat, n (%)	60 (49,2)	9 (32,1)	51 (54,3)	0,040
TRpat, n (%)	30 (24,4)	5 (17,2)	25 (26,6)	0,305

Note: sPAP - systolic pulmonary artery pressure; ARpat, MRpat, TRpat - aortic, mitral, and tricuspid regurgitation greater than grade 2, respectively.

Throughout the prospective follow-up period, pharmacological treatment was adjusted based on each patient's clinical status and in accordance with the availability of newly approved medications for heart failure management. Particular emphasis was placed on prescribing quadruple therapy, as recommended in contemporary heart failure guidelines.

During the two-year follow-up, 29 patients (23.3%) experienced the primary endpoint - a sustained ventricular tachyarrhythmia episode recorded by the device.

The groups stratified by the occurrence of the primary endpoint were comparable in most clinical and demographic characteristics, as shown in Table 1.

Clinical and Demographic Predictors of VT

The presence of AF of any form increased the likelihood of VT by 3-fold (OR = 3.0; 95% CI: 1.23-7.08; p = 0.01). Moreover, the presence of permanent AF was associated with an even higher risk of life-threatening arrhythmias, increasing the likelihood of VT by more than 4-fold (OR = 4.7; 95% CI: 1.18-19.02; p = 0.018). Clinical data analysis is presented in Table 1. Ischaemic heart disease (IHD) was identified as a potential prognostic factor with borderline statistical significance (OR = 2.95; 95% CI: 0.87-4.72; p = 0.10). Other clinical parameters did not show statistically significant associations with VT development in univariate analysis.

Electrocardiographic Predictors of VT

A total of 15 ECG parameters were analysed (see Table 2). Patients with longer QRS durations were less likely to develop VT (p = 0.007). The presence of complete left bundle branch block (CLBBB) based on Strauss criteria was associated with a ~2-fold reduction in VT risk (OR = 0.43; 95% CI: 0.183-1.00; p = 0.049).

We also analysed the modified QRS duration (QRSm) parameter described by N. Varma et al. [12], calculated as the ratio of QRS duration to left ventricular end-diastolic volume (LVEDV). ROC analysis identified a threshold value of 0.6. QRSm values above 0.6 were significantly associated with a reduced risk of VT (OR = 0.40; 95% CI: 0.167-0.993; p = 0.045), reducing the likelihood of life-threatening arrhythmias by approximately 6-fold.

Echocardiographic Criteria

According to univariate analysis (Table 3), the presence of mitral regurgitation (MR) ≥ grade 2 significantly reduced the likelihood of VT (OR = 0.43; 95% CI: 0.164-0.973; p = 0.04). Larger volumes and dimensions of the left atrium (LA) (p = 0.03), medial-lateral LA diameter (p

Table 4.

Multivariable Analysis of Blood Biomarkers

Biomarker	All patients (n=124)	Patients with VT (n=29)	Patients without VT (n=95)	P
Haemoglobin, g/L	133,5 (109-147)	135 (127-146)	132 (109-147)	0,577
NT-proBNP, pg/mL	2268 (1204-4805)	2100 (1064-4177)	2476 (1267-5537)	0,347
NT-proBNP > 2000, n (%)	32 (57,1)	11 (55)	21 (58,3)	0,809
NT-proBNP > 3000, n (%)	22 (39,3)	8 (40)	14 (38,9)	0,935
sST-2, ng/mL	27,1 (17,2-54,8)	39,2 (21,4-64,5)	26,8 (16,4-45,1)	0,154
sST-2 > 35, n (%)	21 (42)	8 (57,1)	13 (36,1)	0,176
Galectin-3, ng/mL	124,5 (115,1-139,9)	137,1 (126-142,65)	118,8 (114,9-132,2)	0,051
Galectin-3 > 12 ng/mL, n (%)	28 (57,1)	12 (80)	16 (47,1)	0,032
CKD-EPI, mL/min/1.73 m²	68 (60,2-77,4)	71,15 (64-88)	67,2 (60-76)	0,247
C-reactive protein (CRP), mg/L	7 (4-10)	8 (5-9)	6,62 (3,34-10,94)	0,454

Table 5.

Predictor Analysis of Ventricular Tachycardia

	Univariate Analysis			Multivariate Analysis		
	OR	95% CI	P	OR	95% CI	P
Predictors						
Presence AF	3	1.23-7.08	0.01	4	1.456-11.1	0.007
Presence IHD	2.95	0.867-4.718	0.1	2.8	1.027-7.626	0.067
Electrocardiographic Criteria						
QRSm ≥0,6	0.4	0.167-0.993	0.045	0.187	0.064-0.55	0.002
LBBB#	0.43	0.183-1.00	0.049	0.82	0.279-2.408	0.718
Echocardiographic Criteria						
GLS ≤6%	13.3	1.364-130.3	0.008	2.38	0.84-6.84	0.228
Mitral regurgitation > 2	0.43	0.164-0.973	0.04	0.285	0.104-0.778	0.014
Laboratory Criteria						
Galectin-3 > 12 ng/mL	4.5	1.073-18.865	0.032	2.37	0.84-6.837	0.102

= 0.037), and right atrium (RA) (p = 0.017) were all associated with an increased risk of VT.

The indexed left ventricular end-systolic dimension (iLVESD) showed a statistically significant protective association, with higher values correlating with lower VT risk (p = 0.02). Likewise, higher systolic pulmonary artery pressure (sPAP) was also associated with reduced VT risk (p = 0.014).

LVEF showed a trend toward statistical significance (p = 0.095), with higher LVEF values observed in patients who experienced VT episodes.

The global longitudinal strain (GLS) parameter was statistically significant (p = 0.014), with lower absolute GLS values observed in patients with VT. ROC analysis validated a GLS cut-off of >-6%; using this threshold in univariate analysis confirmed a statistically significant association (OR = 13.3; 95% CI: 1.364-130.3; p = 0.008).

Biomarkers Associated with VT Risk

Among the laboratory biomarkers analysed (Table 4), galectin-3 showed a near-significant difference in univariate analysis (p = 0.051). Higher values were observed in patients who developed VT. After establishing a threshold value of 12 ng/mL, a statistically significant difference was found (OR = 4.5; 95% CI: 1.073-18.865; p = 0.032). Galectin-3 levels above 12 ng/mL were associated with a 4.5-fold increased risk of VT. This threshold was identified via ROC analysis (sensitivity: 80%, specificity: 53%). Other biomarkers evaluated did not show statistically significant associations with the primary endpoint.

Multivariate Analysis of VT Predictors

During the univariate analysis, seven nominal factors with the highest predictive potential for reaching the primary endpoint were selected (Table 5). These included clinical variables (presence of IHD and AF); electrocardiographic criteria (a modified QRS value greater than 0.6, presence of CLBBB according to the Strauss criteria); echocardiographic criteria (GLS ≥ -6%, presence of mitral regurgitation [MR] of grade 2 or higher); and laboratory indicators (galectin-3 ≥ 12 ng/mL). Based on these variables, a prognostic model was constructed using binary logistic regression to estimate the two-year likelihood of VT in patients with indications for CRT device implantation.

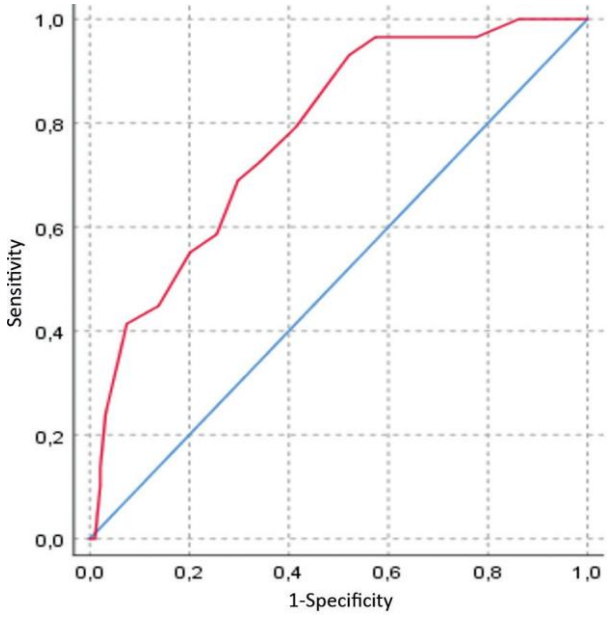

Fig. 1. ROC curve representing the relationship between the 2-year probability of VT and the value of the regression function.

Although the presence of CLBBB according to the Strauss criteria demonstrated statistical significance in the univariate analysis, it was not retained in the final model. The resulting regression equation is as follows: y = -1.337 + 1.029×IHD + 1.438×AF + 0.874×Galectin-3 >12 ng/mL + 0.863×GLS ≤ -6% - 1.676×QRSm ≥ 0.6 - 1.257×MR ≥ 2.

The regression model was statistically significant (p = 0.001). According to the Nagelkerke R^2 coefficient, 28.6% of the variance in the dependent variable (probability of VT occurrence) was explained by the variance in the studied factors. At a cut-off value of 0.228 for the regression function, the model demonstrated a diagnostic accuracy of 73.6%, with a sensitivity of 86.2% and specificity of 69.6%. The area under the ROC curve (AUC), reflecting the relationship between the two-year VT prognosis and the regression function value, was 0.779, which, according to standard expert scales for AUC, indicates good model performance (Figure 1).

DISCUSSION

Over the two-year follow-up period, the primary endpoint was recorded in 29 patients (23.3%), which is comparable with previously published data [13]. The relatively low rate of justified electrical therapy indicates certain limitations in the current criteria used for risk stratification. The relevance of this issue has led to the development of several prognostic models, including the MADIT-ICD Benefit Score, the ESTIMATED Score, and the Seattle Heart Failure Model [14-17]. These tools have demonstrated some effectiveness in prioritising device implantation based on the estimated risk of SCD.

It should be noted that while some of these models include patients with indications for CRT, only the MADIT-CRT study conducted a separate analysis of this subgroup [18]. Patients eligible for CRT represent a specific cohort. If a positive response to CRT is achieved, a significant reduction in the risk of life-threatening ventricular arrhythmias may be observed, as supported by several studies [18, 19]. This suggests that arrhythmic risk reduction may be one of the potential beneficial effects of CRT. Therefore, in the present study, the primary endpoint was defined specifically as the risk of SCD, since this factor determines the choice between CRT-pacemaker (CRT-P) and CRT-defibrillator (CRT-D) implantation. It is evident that predictors of CRT response may also influence the risk of SCD.

The following were identified as independent risk factors for SCD: presence of AF, QRSm >0.6, and MR of grade >2. The prognostic factors included in the multivariate model warrant further discussion.

Among the clinical predictors included in the model were the presence of AF and IHD. The association of AF with increased SCD risk is consistent with published data [20]. AF contributes to increased rate and irregularity of ventricular contractions, thereby reducing myocardial refractoriness and creating conditions conducive to VTde-

velopment [21]. AF is also associated with left ventricular myocardial fibrosis [22], which acts as a substrate for arrhythmias. Additionally, AF has been shown to negatively affect CRT efficacy, potentially amplifying SCD risk [23]. IHD, the second clinical predictor, is a well-established risk factor for SCD [24]. The mechanisms underlying VT in IHD are multifactorial. Acute ischaemic events lead to metabolic and ionic disturbances in the myocardium, resulting in myocyte membrane depolarisation, conduction slowing, and refractoriness prolongation. These changes promote triggered activity and re-entry mechanisms [25]. Subsequently, scar formation in peri-infarct areas provides the anatomical substrate for re-entry, significantly increasing VT risk [26]. Thus, IHD contributes both triggers and substrates for arrhythmogenesis.

The electrocardiographic parameter QRSm >0.6 emerged as a significant predictor in our multivariate model, surpassing the classic Strauss criteria for CLBBB. First described by N. Varma et al. [12], this index has a solid electrophysiological rationale. A 10 ms increase in QRS duration correlates with an 8.3% increase in LV myocardial mass, a 9.2% increase in LV end-diastolic volume, and a 7.8% increase in end-systolic volume [27]. Therefore, QRSm may reflect pronounced LV remodelling with true dyssynchrony, which is relevant when selecting CRT strategy. In our study, higher QRSm values were associated with a lower SCD risk, possibly due to CRT's favourable impact on arrhythmic risk.

Among echocardiographic predictors, mitral regurgitation of grade >2 and GLS below -6% were included in the model. Significant MR may indirectly indicate mechanical dyssynchrony due to asynchronous papillary muscle contraction [28]. This confirms the presence of electromechanical disturbances, which can potentially be corrected by CRT, thereby reducing arrhythmic risk. Although reduced LVEF is widely recognised as a major SCD risk factor [11], it did not demonstrate statistical significance in our study. This may be due to the fact that all patients received CRT-D implantation, making LVEF a potentially modifiable parameter in this context. GLS was found to be a significant predictor, with values below -6% associated with increased SCD risk. Similar findings were reported in a MADIT-CRT subanalysis, where low GLS increased the risk of VT in patients with LVEF <30%, but this correlation was absent in those with LVEF >30% [29]. GLS reduction reflects impaired longitudinal contractility, which may be associated with myocardial fibrosis, ischaemia, and remodelling - known substrates for arrhythmias. Additionally, reduced GLS may signal increased mechanical dispersion, which is also linked to elevated arrhythmic risk [30]. One important limitation of GLS use is the absence of standardised cut-off values, which vary from 6% to 10% across studies [31]. Some publications also examine the role of regional strain in specific LV segments [32]. In our study, only global strain was analysed.

Galectin-3 was the only biomarker significantly associated with the primary endpoint. It plays a key role in fibrosis, inflammation, and myocardial remodelling in CHF. The CARE-HF study demonstrated that elevated galectin-3 levels are linked with adverse outcomes, including death and hospitalisation for CHF decompensation [33]. However, no association between galectin-3 levels and CRT response was found. Conversely, H. Makimoto et al. showed that elevated galectin-3 levels were associated with a higher risk of VT [34]. Nonetheless, galectin-3 use is limited by its lack of myocardial fibrosis specificity, the absence of standardised assays, and inconsistent cut-off values [35]. Despite these limitations, galectin-3 remains a promising biomarker for VT risk stratification and warrants further investigation.

Study limitations

The present study has several limitations. It was a single-centre study with a limited sample size and lacked an external validation cohort. The primary endpoint was based on data from device programming, which may affect arrhythmia detection accuracy. The detection thresholds for VT could have influenced the sensitivity to slower arrhythmic episodes.

CONCLUSION

This study identified several independent predictors of SCD risk in patients implanted with CRT-D devices and enabled the development of a multivariate prognostic model. The findings highlight the potential for creating a personalised device selection algorithm based on routinely available clinical, instrumental, and laboratory data. Novel selection criteria, such as the QRSm index, were proposed and their impact on SCD risk was assessed. Thus, the results contribute to a more individualised approach to SCD risk stratification and device selection in patients with chronic heart failure and reduced left ventricular ejection fraction.

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