Perspectives on the Use of Transthoracic Echocardiography Results for the Prediction of Ventricular Tachyarrhythmias in Patients with Non-ischemic Cardiomyopathy

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Aim. To perform a comparative analysis of indicators of transthoracic echocardiography (TE), to establish echocardiographic predictors and their predictive role in the occurrence of stable ventricular tachyarrhythmia (VT) paroxysms in patients with nonischemic chronic heart failure (HF) and cardioverter-defibrillator (ICD) implanted for primary prevention of sudden cardiac death.

Material and Methods. A prospective study was carried out, which included 166 patients with nonischemic HF at the age of 54 (49; 59) years with the left ventricle ejection fraction (LV EF) ⩽35% and an ICD implanted. The observation time was 24 months. The primary endpoint was the first-ever stable paroxysm of VT (lasting for ⩾30 seconds), detected in the «monitor» zone of VT, or paroxysm of VT, which required ICD therapy.

A total of 34 TE indicators were evaluated. Chi-square, Fischer, Manna-Whitney, single-factor logistic regression (LR), and multi-factor LR were used for data processing and analysis and for predictive modelling. Model accuracy was estimated using 4 metrics: ROC curve area (AUC), sensitivity, specificity and diagnostic efficiency.

Results. During the two-year observation, 32 patients (19.3%) had a primary endpoint. The average time of occurrence of a stable VT episode was 21.6±0.6 months (95% confidence interval [CI] 20.5-22.8 months). The value of LV end-systolic dimension was the only parameter independently associated with VT (odds ratio 2.8 per unit increase, 95% CI 1.04-7.5; p=0.042). The complex analysis of echocardiographic indicators made it possible to identify 5 factors with the greatest predictive potential, which are linearly and nonlinearly related to occurrence of VT. These included the LV end-diastolic and end-systolic volumes, LV mass, index of relative LV wall thickness, upper-lower size of the right atrium. The metrics of the best predictive model were: AUC – 0.71 0.069 with 95% CI 0.574-0.843; specificity 50%, sensitivity 90.9%; diagnostic efficiency 57.1%.

Conclusion. The study made it possible to evaluate the possibilities of the results of TE in predicting the probability of VT occurrence in patients with nonischemic HF and reduced LV EF. Predictive indicators have been identified that can be used to stratify the arrhythmic risk in the exposed cohort of patients.

Keywords: chronic heart failure; ventricular tachyarrhythmia; prognostic models; transthoracic echocardiography.

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Introduction

We know that the occurrence of ventricular tachycardias (VT) and ventricular fibrillation (VF) is a life-threatening condition that can lead to sudden cardiac death (SCD) [1]. The manifestation of these arrhythmias is based on electrophysiological remodeling of the heart, which develops when a morphological substrate appears that predisposes to electrical instability of the myocardium (scar, fibrosis) [2]. According to modern concepts, the group of high arrhythmic risk includes patients with heart failure with a reduced left ventricle (LV) ejection fraction (HFrEF) [3]. Several large studies have shown that implantable cardioverter defibrillators (ICDs) are an effective measure for primary prevention of SCD in this category of patients [4].

In accordance with current clinical guidelines, the LV EF value calculated during transthoracic echocardiography is decisive in deciding whether to implant an ICD in patients with HFrEF who don't have documented persistent VT paroxysms and anamnestic data for a previous SCD episode [3,5]. Meanwhile, only 20-25% of patients with chronic heart failure (CHF) with LV EF ⩽35%, who were implanted with ICD for primary prevention of SCD, receive appropriate life-saving therapy [6,7]. Most patients are doomed to a series of reimplantations (replacement of devices due to depletion of the charge), each of which, on the one hand, increases the financial costs of the state, on the other hand, can be complicated by infection of the implanted device pocket. The expediency of ICD installations is especially acute for patients with non-ischemic HFrEF, who have an even lower incidence of VT [8], and therefore require even more careful selection [9]. Thus, determination of indications for ICD implantation only on the basis of LV EF clearly requires revision and development of new approaches to arrhythmic risk stratification in patients with HFrEF [10].

Echocardiography over the past decades has been one of the leading methods for diagnosing the pathology of the cardiovascular system. The indisputable advantages of the technique are the non-invasive nature of the study, the relatively inexpensive cost and the proven high information content of the results. This method is routine in terms of examining patients with HFrEF and allows us not only to assess the global contractility of the LV myocardium and determine the value of LV EF, but also to provide additional diagnostic information about the structure of the heart, which may have an independent prognostic potential in determining the likelihood of VT occurrence [11].

The aim of this work is to perform a comparative analysis of transthoracic echocardiography indicators, to establish echocardiographic predictors and their prognostic role in the occurrence of persistent paroxysms of ventricular tachyarrhythmias (VT), or VT/VF paroxysms, requiring electrotherapy (anti-tachycardic stimulation or shock therapy) in patients with non-ischemic CHF with LV EF ⩽35% without syncope or persistent ventricular arrhythmias in history.

Material and methods

This study was performed in accordance with Good Clinical Practice and the principles of the Declaration of Helsinki. The design of the study was approved by the local ethics committee of the Federal State Budgetary Educational Institution of the Astrakhan State Medical University of the Ministry of Health of Russia (Minutes No. 3 of the LEC meeting dated December 30, 2021). All patients under follow-up signed an informed consent to participate in the study.

Selection of patients

The selection of patients was carried out from 2013 to 2021. A total of 540 patients with HFrEF were selected for ICD implantation as a means of primary prevention of SCD. All patients were diagnosed with dilated cardiomyopathy after excluding other diseases that can lead to CHF. A total of 166 patients completed the full protocol of postoperative follow-up (Fig. 1).

Criteria for inclusion in the study: LV EF ⩽35%; NYHA class III-IV CHF against the background of optimal drug therapy for the last 6 months; the absence of documented persistent paroxysms of VT/VF, anamnestic data for a previous episode of SCD.

Criteria for exclusion from the study: the presence of a lesion of the coronary arteries according to coronary angiography; hypertrophic cardiomyopathy; arrhythmogenic dysplasia of the right ventricle; valvular heart disease; verified hereditary channelopathies.

Implantation and ICD programming

All patients included in the study were implanted with ICD as a means of primary prevention of SCD

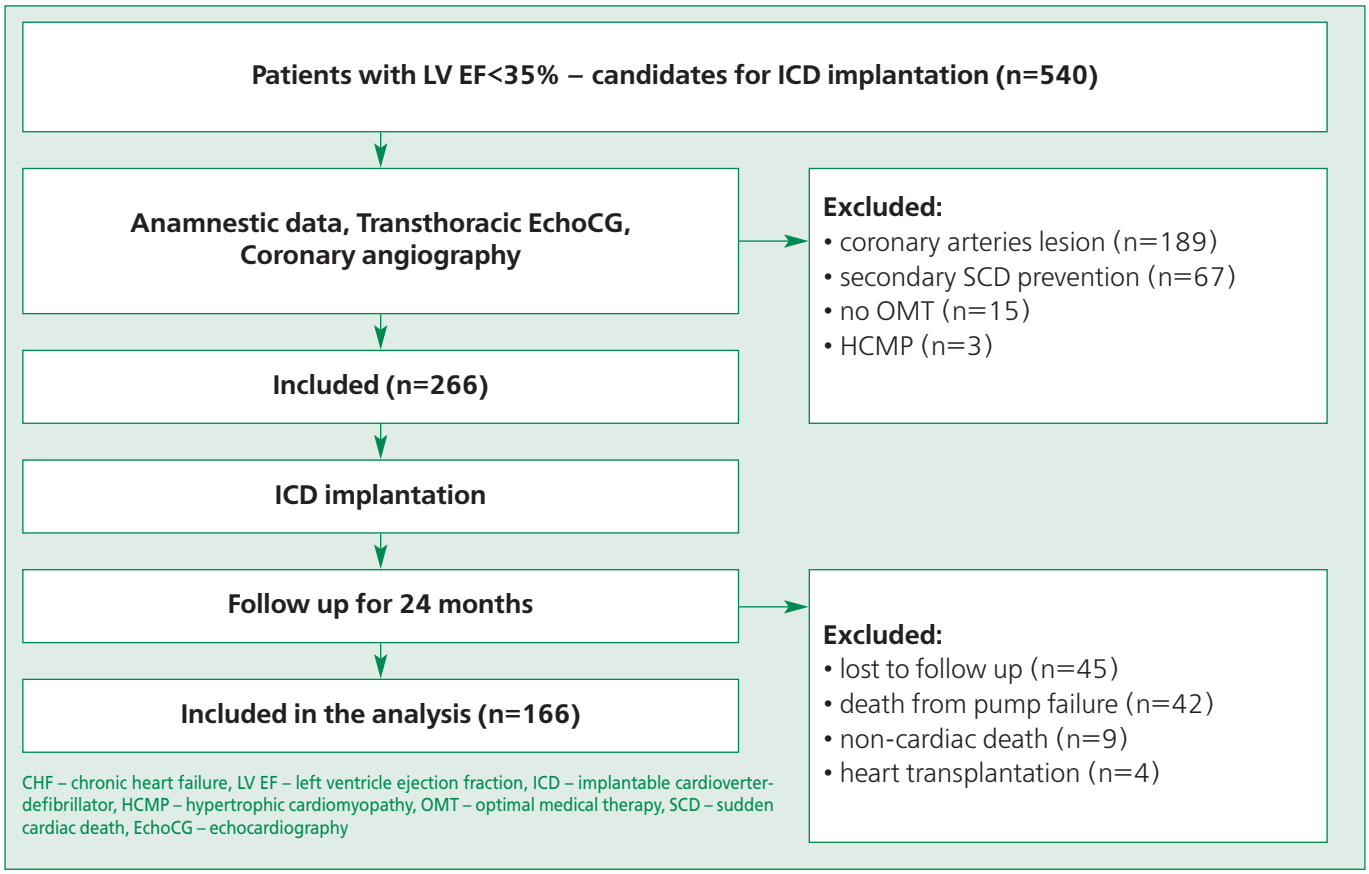

Figure 1. Flowchart diagram representing the study design

[3,4]. ICD with the function of cardiac resynchronization therapy (CRT-D) was implanted in 55% of cases (n=91) due to the presence of severe intraventricular conduction disturbances. Device implantation was carried out according to accepted methods [12,13]. A bipolar or quadripolar left ventricular electrode was implanted using a delivery system into one of the coronary sinus veins. The lateral vein of the heart was preferred for implantation, usually located above the zone of late activation of the left ventricle in patients with complete left bundle branch block.

ICD programming was performed intraoperatively, on days 4-5 and 3 months after device implantation, then once every 12 months. The software algorithms developed by manufacturers of implantable electronic devices were used for this procedure.

The parameters set for stimulation were selected based on the need to treat bradycardia (in patients with ICD without CRT function). A vector with a lower stimulation threshold and no phrenic nerve stimulation was chosen in the case of CRT-D implantation to provide LV stimulation. The selection of atrioventricular delay was carried out in such a way as 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 ECG. Manufacturers' automatic algorithms were used when it was possible to select delays [14].

Two-zone programming (VT zone=160 beats/min, VF zone=200 beats/min) with activation of supraventricular tachyarrhythmia discrimination algorithms was used to detect ventricular arrhythmias (primary endpoint). ICD programming was carried out in such a way as to minimize the likelihood of inappropriate ICD triggering and, if possible, replace high-voltage shocks with antitachycardia pacing (ATP). In accordance with the Expert Consensus on Optimal ICD Programming and Testing [15], the VT zone was programmed as a «monitor» zone in some patients, that is, detection of ventricular arrhythmias was carried out when registering spontaneous activity in this zone, but electrotherapy (antitachycardia pacing or shock therapy) was not was carried out.

Table 1. Echocardiographic parameters defined as dichotomous indicators (labelled as "pat")

	$iEDR_{pat}$		$iESR_{pat}$		$LVPW_{pat}$		TIS_{pat}		$iRWTLV_{pat}$
	men	women	men	women	men	women	men	women	
Value	>3.1 sm/m²	>3.2 sm/m²	>2.1 sm/m²	>2.1 sm/m²	>1 см	>0.9 sm	>1 sm	>0.9 sm	>0.42

iEDR – indexed end-diastolic size, iESR – indexed end-systolic size, LVPW – thickness of the posterior wall of the left ventricle, TIS – thickness of the interventricular septum, iRWTLV – index of relative wall thickness of the left ventricle, «pat» are the values of the corresponding indicators that exceed the upper threshold of the reference range

Postoperative follow-up

The patients included in the study were followed up for 2 years. When choosing the duration of follow-up, we were guided by the results of previously published studies indicating that in most cases the first episode of appropriate electrotherapy in patients with HFrEF with ICDs implanted for primary prevention of SCD occurs within 1-2 years after device implantation [6,16].

Patients were invited to visit the clinic 3-12-24 months after implantation. During the follow-up, events detected by the implanted device and included in different detection zones were recorded in patients during ICD programming visits. Appropriate electrotherapy with recording the episode in the ICD memory was used depending on the installed program of the implanted device, subject to the conditions of the rhythm rate, tachycardia stability and the use of tachyarrhythmia discrimination algorithms, which allowed us to evaluate each episode in detail, taking into account the stored electrograms. We assessed the date of onset of the VT/VF episode, the adequacy of the rhythm discriminators, and the advisability of using electrotherapy.

Half of the patients (n=80) underwent remote ICD monitoring (Medtronic Carelink, Biotronik Home Monitoring). Remote alerts were configured to inform the doctor about the occurrence of signs of possible electrode dysfunction and the registration of paroxysms of arrhythmias, including those requiring electrotherapy.

Echocardiogram analysis

Before or immediately after implantation, two experts performed transthoracic echocardiography on all patients before or immediately after implantation using an expert-class Philips EPIQ 5 ultrasound machine according to a standard protocol using the following methods: two-dimensional echocardiography, M-mode, Doppler echocardiography (pulsed and continuous wave Doppler mode), color Doppler mode blood flow mapping. We received standard transthoracic projections and sections in all patients. We used synchronous recording with an electrocardiogram to determine the phases of the cardiac cycle. We recorded on the hard disk of the ultrasonic machine for subsequent viewing and frame-by-frame analysis of various parameters of the patient's beating heart in real time and in real time. During echocardiography, we determined the shape and size of the heart chambers, intracardiac structures, aorta and pulmonary artery, and excluded the presence of congenital and acquired anomalies of the heart structures.

We determined the dimensions of the left atrium: anterior-posterior (LA_{ap}), medial-lateral (LA_{ml}) and superior-inferior (LA_{si}), LA volume (VLA); right atrium: medial-lateral (RA_{ml}) and superior-inferior (RA_{si}); right ventricle; thickness of the interventricular septum (TIS); posterior wall of the left ventricle (LVPW); linear dimensions of the LV: end-systolic (ESR) LV and end-diastolic LV (EDR); volumetric characteristics of the left ventricle: end-systolic volume (ESV) and end-diastolic volume (EDV); indexed indicators of linear and volumetric measurements of the left ventricle: iESR, iEDR, iESV, iEDV; LV EF [17]. Indicators were considered different from the norm (marking «pat») with values exceeding the standards (Table 1).

Based on the data on the systolic pressure gradient across the tricuspid valve (SPGTV) and pressure in the right atrium (RAP), we calculated the level of systolic pressure in the pulmonary artery (SPPA) using the formula: SPPA = SPGTV + RAP. RAP was determined taking into account the diameter and degree of collapse of the inferior vena cava: 0-5 mm Hg with a normal diameter of the inferior vena cava and collapse of the vein on inspiration >50%; 10 mm Hg with vein dilatation and preserved collapse; 15 mmHg with vein expansion and collapse <50%; 20 mm Hg when the vein is dilated and its diameter doesn't change during inspiration.

The mean wall thickness of the LV (MWTLV) was calculated using the formula: MWTLV = (TIS+LVPW)/2. The relative wall thickness index of the left ventricle (iRWTLV) was calculated using the formula: iRWTLV = (2×LVPW)/ EDR. LV myocardial mass (LVMM) was calculated using the formula: LVMM = 0.8×(1.04×[(EDR+LVPW+TIS)^3 – (EDR)^3]) + 0.6 and indexed to body surface area (iLVMM). LVMI values greater than 115 g/m^2 in men and greater than 95 g/m^2 in women were considered as signs of LV hypertrophy. An increase in LVMI above these values at iRTLV>0.42 ($iRTLV_{pat}$) diagnosed concentric hypertrophy, we determined eccentric hypertrophy with an increase in LVMI at iRTLV⩽0.42, and we verified the presence of concentric LV remodeling in the case of normal values of LVMI and iRTLV>0.42 [17].

An increase in LA (LA_{pat}) was established at LAsi>5 cm and LA_{ml}>4 cm, RA was considered increased (RA_{pat}) at LA_{si}>4.6 cm and RA_{ml}>3.9 cm.

We assessed the function of the mitral, tricuspid and aortic valves. The presence of regurgitation of any degree on the aortic valve (AR_{pat}), the second and higher degree on the mitral and tricuspid valves (MR_{pat} and TR_{pat}, respectively) was considered pathological.

Study endpoints

The primary endpoint was first-time sustained VT paroxysm (lasting ⩾30 seconds) detected in the «monitor» zone of VT, or VT/VF paroxysm requiring electrotherapy (antitachycardia pacing or shock therapy).

Statistical analysis

The materials of this study were subjected to statistical processing using the methods of parametric and non-parametric analysis. Accumulation, correction, systematization of initial information and visualization of the obtained results were carried out in Microsoft Office Excel 2010 spreadsheets. Statistical analysis was carried out using the IBM SPSS Statistics 23 program. The description and comparison of quantitative indicators was carried out taking into account the distribution, the correspondence of which to the normal one was assessed using the Kolmagorov-Smirnov's test. Data when confirming the normality of the distribution were described using the arithmetic mean (M) and standard deviation (SD). Comparison was performed using Student's t-test. The values of the median (Me), lower and upper quartiles (Q_1; Q_3) were indicated in the absence of normal distribution, the indicators were compared using the Mann-Whitney's test. Comparison of indicators measured in the nominal scale was carried out using Pearson's χ^2 test. We used the odds ratio (OR) with 95% confidence interval (CI) as a quantitative measure of the effect when comparing relative rates. The significance of the factor was considered proven if the confidence interval was found outside the no-effect limit, which was taken as 1. The critical level of significance when testing statistical hypotheses was taken equal to 0.05.

The construction of a multivariate prognostic model to determine the two-year probability of VT occurrence in patients HFrEF based on the parameters studied by echocardiography was performed using the binary logistic regression method. The selection of independent variables was carried out by the method of stepwise inverse selection using Waldovsky's statistics as an exclusion criterion. The statistical significance of the resulting model was determined using the χ^2 test. Nigelkirk's R^2 indicator served as a measure of certainty indicating that part of the variance that can be explained by logistic regression. We performed a ROC analysis with calculation of the curve area (AUC) to assess the predictive value of the model and find the threshold value of the resulting function at the cut-off point.

Results

The main clinical and demographic indicators of patients included in the study are presented in Table. 2.

Table 2. Clinical and demographic characteristics of patients included in the study

Clinical indicator	Indicator value
Age, years	54 (49; 59)
Male gender, n (%)	125 (75)
Hypertension, n (%)	76 (46)
Diabetes mellitus, n (%)	22 (13)
Obesity, n (%)	66 (40)
Cerebral stroke, n (%)	13 (8)
CKD, n (%)	76 (46)
Unsustainable VT, n (%)	10 (6)
AF (paroxysmal/persistent), n (%)	38 (23)
AF (permanent), n (%)	8 (5)

Data are presented as Me (Q1; Q3) unless otherwise noted.

CKD – chronic kidney disease, VT – ventricular tachyarrhythmias, AF – atrial fibrillation

Table 3. Echocardiographic parameters studied depending on the achievement of the endpoint

Echocardiographic parameters	All patients (n=166)	Patients without VT (n=134)	Patients with VT (n=32)	p*
EDV, ml	240 (204; 299)	238 (205; 296)	234 (208; 298)	0.72
iEDV, ml/m^2	124 (102; 147)	117 (100; 147)	125 (105; 154)	0.25
ESV, ml	165 (139; 211)	162 (139; 208)	173 (137; 208)	0.61
iESV, ml/m^2	83 (69; 106)	82 (67; 106)	96 (78; 119)	0.29
EDR, sm	6.8 (6.3; 7.4)	6.7 (6.2; 7.4)	6.7 (6.4; 7.3)	0.34
iEDR, sm/m^2	3.5 (3.0; 3.9)	3.5 (3.0; 3.8)	3.6 (3.3; 4.0)	0.11
ESR, mm	5.9 (5.6; 6.5)	6 (5.3; 6.5)	5.9 (5.8; 6.3)	0.37
iESR, cm/m^2	3.1 (2.7; 3.4)	2.9 (2.6; 3.3)	3.1 (2.9; 3.5)	0.042
TIS, sm	1.0 (0.8; 1.2)	1.0 (0.8; 1.2)	1.0 (0.9; 1.2)	0.98
LVPW, sm	1.1 (1.0; 1.2)	1.1 (0.9; 1.2)	1.0 (1.0; 1.2)	0.93
AvLVW, sm	0.9 (1.0; 1.2)	1.0 (0.9; 1.2)	1.0 (0.9; 1.2)	0.88
iRWTLV, sm	0.31 (0.26; 0.36)	0.31 (0.25; 0.36)	0.30 (0.26; 0.33)	0.56
EF Simpson, %	29 (25; 34)	29 (25; 35)	27 (22; 31)	0.42
LVMM, g	333 (276; 377)	319 (257; 371)	350 (276; 409)	0.43
iLVMM, g/m^2	168 (141; 196)	167 (136; 185)	169 (156; 232)	0.16
LA_{ap}, sm	6.0 (5.4; 6.5)	6.0 (5.4; 6.6)	5.9 (5.4; 6.5)	0.93
LA_{ml}, sm	4.7 (4.3; 5.4)	4.8 (4.4; 5.4)	4.6 (4.3; 5)	0.53
LA_{si}, sm	4.7 (4.3; 5.2)	4.7 (4.3; 5.3)	4.7 (4; 5.2)	0.47
VLA, ml	103 (78; 127)	105 (81; 127)	79 (70; 119)	0.22
RA_{ml}, sm	5.2 (4.5; 6.0)	5.6 (4.7; 6.0)	4.8 (4.4; 5.5)	0.06
RA_{si}, sm	4.0 (3.6; 4.4)	4.1 (3.7; 4.6)	3.8 (3.3; 4.4)	0.09
SPPA, mm Hg	45 (36; 57)	47 (39; 59)	38 (30; 55)	0.26
Concentric LV hypertrophy, n (%)	22 (13)	17 (13)	5 (16)	0.92
Eccentric LV hypertrophy, n (%)	144 (87)	117 (87)	27 (84)	0.92
RA_{ap}, n (%)	82 (49)	68 (51)	14 (44)	0.61
LA_{ap}, n (%)	129 (78)	105 (78)	24 (75)	0.72
AR_{pat}, n (%)	3 (2)	1 (1)	2 (6)	0.41
MR_{pat}, n (%)	118 (71)	96 (72)	22 (69)	0.53
TR_{pat}, n (%)	55 (33)	47 (35)	8 (25)	0.43
$iEDR_{pat}$, n (%)	125 (75)	95 (71)	30 (94)	0.07
$iESR_{pat}$, n (%)	161 (97)	129 (96)	32 (100)	0.9
$LVPW_{pat}$, n (%)	97 (58)	76 (57)	21 (66)	0.78
TIS_{pat}, n (%)	84 (51)	67 (50)	17 (53)	0.83
$iRWTLV_{pat}$, n (%)	22 (13)	17 (13)	5 (16)	0.55

* - when comparing patients without VT with patients with VT

Data are presented as Me (Q1; Q3) unless otherwise noted.

EDV – end-diastolic volume, iEDV – indexed end-diastolic volume, ESV – end-systolic volume, iESV – indexed end-systolic volume, EDR – end-diastolic size, iEDR – indexed end-diastolic size, ESR – end-systolic size, iESR – indexed end-systolic size, TIS – thickness of the interventricular septum, LVPW – thickness of the posterior wall of the left ventricle, AvLVW – the average wall thickness of the left ventricle, iRWTLV – index of relative wall thickness of the left ventricle, EF – ejection fraction, LVMM – left ventricular myocardial mass, iLVMM – left ventricular myocardial mass index, LA_{ap} – anterior-posterior size of the left atrium, LA_{ml} – medial-lateral size of the left atrium, LA_{si} – superior-inferior size of the left atrium, VLA – left atrial volume, RA_{ml} – medial-lateral size of the right atrium, RA_{si} – superior-inferior size of the right atrium, AR_{pat} – pathological regurgitation on the aortic valve, MR_{pat} – pathological regurgitation on the mitral valve, TR_{pat} – pathological regurgitation on the tricuspid valve, $iEDR_{pat}$, $iESR_{pat}$, $LVPW_{pat}$, TIS_{pat}, $iRWTLV_{pat}$ are the values of the corresponding indicators that exceed the upper threshold of the reference range (see Table 2). LA_{ap} was determined at LA_{si}>5 cm and LA_{ml}>4 cm, RA_{ap} was determined at RA_{si}>4.6 cm and RA_{ml}>3.9 cm.

Table 4. Relationship between the investigated factors and the study endpoint

Factors	Univariate analysis			Multivariate analysis		
	OR	95% CI	p	OR	95% CI	p
iESR	2.80	1.04-7.50	0.042	–	–	–
$iEDR_{pat}$	2.40	0.94-5.90	0.070	–	–	–
RA_{si}	0.54	0.29-1.03	0.060	0.17	0.04-0.70	0.014
EDV	1.002	0.99-1.01	0.420	0.93	0.88-0.98	0.011
ESV	1.003	0.99-1.01	0.360	1.10	1.01-1.14	0.034
iRWTLV	0.024	0.001-17.6	0.270	0.0001	0.0001-0.74	0.046
LVMM	1.004	0.99-1.01	0.180	1.02	1.00-1.03	0.016

OR – odds ratio, CI – confidence interval, iESR – index of end-systolic size, $iEDR_{pat}$ – the value of the index of end-diastolic size, exceeding the upper threshold of the reference range (see Table 2); EDV – end-diastolic volume, ESV – end-systolic volume, iRWTLV – index of relative wall thickness of the left ventricle, LVMM – left ventricular myocardial mass, RA_{si} – superior-inferior size of the right atrium

In general, an increase in the linear and volumetric dimensions of the LV and a significant decrease in LV EF was characteristic of the studied cohort of patients (Table 3). Pathological LV remodeling by the type of eccentric hypertrophy prevailed (n=144; 87%). Approximately half of the patients included in the study had an increase in the thickness of the TIS and LVPW (51% and 58%, respectively). Pathological mitral regurgitation was more often determined against the background of atriomegaly (71% vs 33% of patients with tricuspid regurgitation).

During the two-year follow-up, the primary end point was registered in 32 patients (19.3%). The mean time to onset of a sustained episode of VT was 21.6±0.6 months (95% CI=20.5-22.8 months).

The groups formed depending on the achievement of the end point differed statistically significantly in iEDR value (p=0.042). Differences between groups in $iEDR_{pat}$, RA_{si} iRA_{ml} values were close to critical (p=0.07; p=0.06; p=0.09, respectively).

Univariate analysis showed that an increase in the iESR value by each unit increased the chances of developing VT by almost 3 times (OR=2.8; 95% CI=1.04-7.5; p=0.042).

Prognostic models based only on linear, volumetric and dichotomous characteristics of the left ventricle had a low sensitivity (not higher than 6%). When we added the dimensions of LA and RA, VLA, SPPA and the dichotomous indicators AR_{pat}, MR_{pat}, TR_{pat} to the multivariate model, we obtained a predictive model that can be described by the following equation (1):

$$p = 1/(1+e^{-z})\times 100\%$$
$$z = 13.1-0.8\times X_{EDR}+0.7\times X_{ESR}-15.4\times X_{iRWTLV}-1.8\times X_{RAsi}+0.02\times X_{LVMM} \quad (1),$$

where p is the two-year probability of VT, X_{EDR} is the LV end-diastolic volume, X_{ESR} is the LV end-systolic volume, X_{iRWTLV} is the value of the relative LV wall thickness index, X_{RAsi} is the superior-inferior limit of the right atrium, X_{LVMM} is the left ventricular myocardium mass, e is a mathematical constant approximately equal to 2.71828.

Based on the values of the regression coefficients, the echocardiographic parameters LV ESV, LVMM have a direct relationship, and the LV EDV, iRWTLV, RA_{si} parameters have an inverse relationship with a two-year probability of VT. The resulting regression model is statistically significant (p=0.003), and, like each of the parameters included in the model, has a statistical significance level (Table 4).

Based on the value of the Nigelkirk determination coefficient, model (1) takes into account 41.8% of the factors that determine the two-year probability of occurrence of VT in patients with HFrEF of non-ischemic origin. Diagnostic efficiency was 88.9% (sensitivity – 45.5%, specificity – 98.1%).

The area under the ROC curve, corresponding to the relationship between the two-year forecast of VT and the value of the regression function, was 0.71±0.069 with 95% CI=0.574-0.843 (Fig. 2).

The threshold value of function (1) at the cut-off point was 0.0521. Values equal to or greater than this value corresponded to the forecast of occurrence

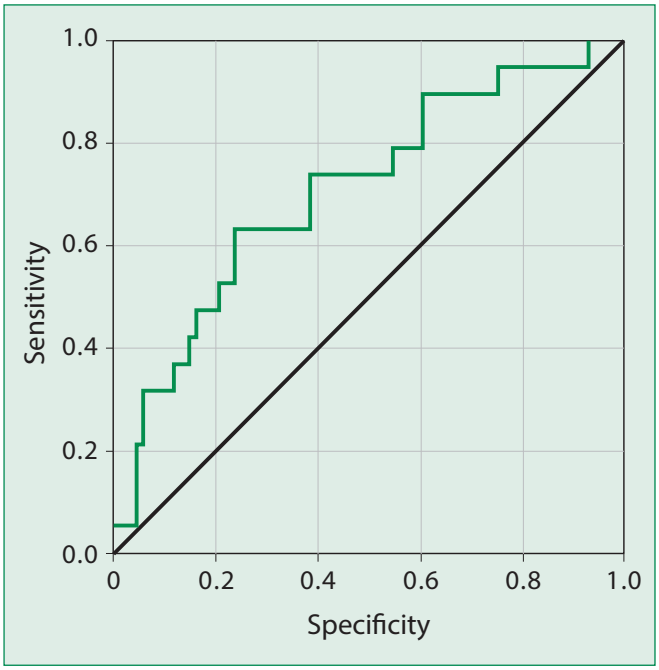

Figure 2. Receiver operating characteristic curve (ROC) for prediction of ventricular tachyarrhythmias based on the prognostic model (1)

of VT within the next 2 years. The sensitivity and specificity of the method were 78.9% and 54.4%, respectively.

After adjusting the classification threshold, the diagnostic efficiency of the resulting predictive model was 57.1% (sensitivity 90.9% specificity 50%) based on the results of the ROC curve analysis.

Discussion

We note that the works devoted to the search for echocardiographic parameters associated with arrhythmic risk in patients with HFrEF are not numerous. Most of them, as VT predictors, study the parameters of the latest echocardiographic methods for studying myocardial movement in real time (tissue Doppler, two-dimensional deformation technology), which undoubtedly improve the accuracy of diagnosing the VT/VF substrate. Meanwhile, in our country, traditional echocardiography remains the most accessible method of cardiac imaging, which makes the potential use of routine echocardiographic characteristics for arrhythmic risk stratification relevant and in demand in the clinic.

Echocardiography data obtained before ICD implantation demonstrated that the process of remodeling of the heart chambers was initiated with a significant increase in linear and volume parameters of the left ventricle and atria, diffuse hypokinesis and a significant decrease in LV EF, in all HFrEF patients included in the study. Contrary to this general trend, the degree of arrhythmic risk in the studied patients during the follow-up period was not the same. During the prospective study, the endpoint registration rate during the two-year follow-up was 19%, which indicates the low sensitivity of LV EF as a selection criterion for ICD implantation.

Groups formed depending on the achievement of the end point didn't differ in echocardiographic parameters widely used in practice: EDV, ESV, TIS, WTLV, LVMM, LV EF. The only parameter that acted as an independent predictor of VT was the vESR value, an increase in which by each unit increased the chances of developing VT by almost 3 times (OR=2.8; 95% CI=1.04-7.5; p=0.042). Meanwhile, we observed in the group of patients with VT a trend towards higher vESR and iEDRpat values. These are echocardiography indicators indexed by body surface area, the need for the use of which is noted in the current regulatory documents [18]. J.N. Catanzaro et al. who came to similar results showed that an increase in ESR over 4 cm doubled the odds of VT (OR=2.5; p=0.02) [11]. We can assume that the large linear dimensions of the LV in systole may indicate a more pronounced intraventricular mechanical dyssynchrony, which many researchers consider as an independent predictor of VT/VF induction [19].

In one of the studies devoted to the study of the issue under consideration, we concluded that the frequency of ventricular arrhythmias is higher in the case of diagnosing LV hypertrophy, verified with TIS and LVPW ⩾1.2 cm or an increase in LVMM indexed by growth ⩾163 g/m for men and ⩾121 g/m for women (by 2 and 3 times, respectively) [20]. These indicators are often included in multivariate models [21]. According to our results, LVMM and iRWTLV turned out to be significant factors in the predictive model (p=0.016 and p=0.046, respectively). Probably noteworthy is the fact that almost all of the observed patients had LVMM and iRWTLV values, allowing the LV geometry to be interpreted as eccentric hypertrophy (n=144; 87%). We believe that eccentric and concentric hypertrophy (which was diagnosed in 13% of patients) may indicate a high arrhythmic risk and are associated with SCD [22]. Our study included patients with a significant decrease in LV systolic function, which may require the development of other diagnostic criteria or the description of new

types of remodeling that are more sensitive to the risk of SCD in HFrEF patients.

An interesting finding was the determination of the possible predictive potential of the right atrium size. The relationship between the superior-inferior size and the likelihood of VT was inverse and had a high level of statistical significance (univariate analysis p=0.06; multivariate analysis p=0.014). Despite the fact that both medial-lateral and superior-inferior RA sizes were higher (p<0.1) in the group of patients without VT, the frequency of atriomegaly in both groups was comparable (51% and 45%, respectively, p=0.6). We can assume that the clinical manifestation of atrial remodeling in patients with non-ischemic HFrEF is the occurrence and persistence of atrial fibrillation (AF), which is closely related to the arrhythmogenic variant of SCD [23]. According to our previous results, AF almost 3 times increased the risk of fatal ventricular tachyarrhythmias in HFrEF patients without coronary artery disease [8]. In this study, we didn't find a statistically significant linear correlation between VT/VF frequency and LA and RA sizes. However, the exclusion of these indicators during the logistic regression significantly reduced the diagnostic value of the results.

During the study, we obtained a multivariate prognostic model that includes only echocardiographic parameters. It's important that it was characterized by high sensitivity (90.9%), which allows to verify the high risk of VT/VF with high accuracy. The area under the ROC curve corresponding to the relationship between the two-year forecast of VT and the value of the regression function was 0.710±0.069, which corresponds to the good quality of the prognostic model.

The data presented in the publication are interim results of an ongoing single-center prospective study, which will include at least 450 patients with HFrEF. Undoubtedly, increasing the number of observations as new patients are included may increase the significance of future results. One of the main conclusions of practical importance can be the hypothesis that the two-year probability of occurrence of ventricular tachyarrhythmias in patients with non-ischemic HFrEF can be predicted not only on the basis of the linear and volumetric sizes of the left ventricle. Probably, the echocardiographic characteristics of the atria are also important.

Study limitation

This study has several limitations. These include the small number of enrolled patients and the single center nature of the study.

The end point was assessed based on data from the implanted ICD survey. The limitation for identifying VT episodes was the magnitude of the lower rate of ventricular events detected by the device (this is a ventricular arrhythmia with a rate of less than 160 per minute for all patients). For this reason, VT episodes at a lower frequency may not have been diagnosed.

Half of the patients included in the study (55%) were implanted with CRT-D. The nature of the «response» to this therapy was not studied in this study. The ongoing cardiac resynchronization therapy could potentially modify the primary SCD substrate in some of the observed patients, despite approximately the same distribution of devices in groups formed depending on the occurrence of the primary endpoint.

Conclusion

The echocardiographic picture of patients with non-ischemic HFrEF, in addition to diffuse hypokinesis and a decrease in global LV contractility, includes remodeling of the heart chambers with a significant increase in linear and volumetric parameters of the LV and atria. The LV EF value doesn't allow us to carry out arrhythmic risk stratification within the group of HFrEF patients. According to the results obtained, LV ESR indexed by body surface area is the only independent predictor of ventricular tachyarrhythmias. The use of atrial echocardiographic characteristics as part of multivariate predictive models may be promising to improve the identification of HFrEF patients at high arrhythmic risk.

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