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Clinical predictors of occurrence of ventricular tachyarrhythmias in patients with reduced left ventricle ejection fraction. Results of single-center prospective study

Aim	To evaluate the diagnostic significance of clinical and demographic parameters for predicting a 2-year probability of ventricular tachyarrhythmias (VT) in patients with chronic heart failure and reduced left ventricular ejection fraction (CHFrLVEF).
Material and methods	This single-center, prospective cohort study included 175 patients with CHFrLVEF who were implanted with a cardioverter defibrillator (CD). The endpoint was a CD-detected episode of VT. Patients were followed up for 2 years with visits at 3, 12, and 24 months after CD implantation.
Results	The primary endpoint was observed in 43 (24.4%) patients at an average of 20.9 months (95% confidence interval (CI), 20–21.9). The 2-year risk of fatal ventricular arrhythmias increased with detection of unstable VT (one-factor analysis, odds ratio (OR), 4.2; 95% CI, 1.1–16.5; p=0.041; multifactor analysis, OR, 6.3; 95% CI, 1.5–26.3; p=0.012) and with ischemic CHFrLVEF origin (one-factor analysis, OR, 2.2; 95% CI, 1.1–4.5; p=0.021; multifactor analysis, OR, 2.5; 95% CI, 1.2–5.1; p=0.018). In the presence of any type of atrial fibrillation (AF) in patients with non-ischemic CHFrLVEF, the probability of VT increased threefold (one-factor analysis, OR, 2.97; 95% CI, 1.02–8.8; p=0.047; multifactor analysis, OR, 3.5; 95% CI, 1.1–10.9; p=0.032).
Conclusion	The presence of ischemic heart disease and unstable VT paroxysms can be included in the number of important clinical predictors of VT in patients with CHFrLVEF. In patients with non-ischemic CHF, the presence of AF is associated with a high risk of VT.

Keywords	Heart failure; cardioverter defibrillator; sudden cardiac death; ventricular tachyarrhythmias
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Introduction

Cardiac arrest, comprising a loss of cardiovascular activity resulting from ventricular tachycardia, fibrillation or flutter, is the cause of death in 30–50% of patients suffering from chronic heart failure with reduced ejection fraction (HFrEF). In some cases, a pathophysiological trigger leading to this condition can be identified (myocardial ischemia, catecholamine crisis, critical electrolyte imbalance), but often the cause of acute decompensated heart function remains undiagnosed. [1] The three key scenarios of sudden cardiac death (SCD) in patients with HFrEF are: (1) acute mechanical dysfunction manifested by asystole, bradyarrhythmia and electromechanical dissociation; (2) sustained cardioversion-resistant ventricular fibrillation (VF); (3) myocardial electrical instability manifested by ventricular tachyarrhythmias (VT). These can be effectively reduced by means of anti-tachycardia stimulation or implanted cardioverter-defibrillator (ICD) shocks. ICDs are implanted in patients with reduced left ventricular ejection fraction (LVEF) in order4 to exclude the third scenario of SCD [2]. Although the use of LVEF values as the only high-risk factor for arrhythmia, which requires the implantation of an ICD, is included in the current clinical guidelines [3, 4], this approach has lately been subjected to significant criticism [5, 6].

Potential identifiers of high-risk fatal ventricular arrhythmias (VA) in HFrEF patients may include (but are not limited to) such clinical factors such as atrial fibrillation (AF) [7], coronary artery disease (CAD) [8], obesity [9], chronic kidney failure [10], as well as a history of syncope [11], nonsustained paroxysmal VTs [12] or multi-factor combinations [5]. Given

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the heterogeneity of data available in this respect, we conducted a single-center, prospective cohort study to assess the diagnostic value of clinical and demographic variables for predicting the likelihood of VT in HFrEF patients over the next two years.

Material and methods

The study design was approved by the ethics committee. All patients signed informed consent to be included in the study.

Initially, the study included 220 patients who received ICDs as primary prevention of SCD. A total of 175 patients completed the postoperative follow-up protocol (Figure 1).

Inclusion criteria: LVEF ≤35%; CHF of functional classes (FC) III–IV according to the New York Heart Association (NYHA) classification. Exclusion criteria: documented sustained paroxysmal VT/VFs; history of SCD episode; indications for heart surgery (correction of valvular insufficiency, myocardial revascularization).

The following clinical and demographic characteristics were investigated: age; sex; the presence of coronary artery disease (according to the coronary angiography findings); the presence of postinfarction cardiosclerosis, AF, arterial hypertension, diabetes mellitus, obesity; a history of myocardial stroke (based on anamnestic data); the presence of chronic kidney disease (glomerular filtration rate <60 mL/min/1.73 m^2 continuing for three months or longer, regardless of the presence of other signs of kidney damage); CHA_2DS_2VASc score (calculated irrespective of the presence of AF); surgical revascularization more than three months prior to inclusion in the study; nonsustained paroxysmal VTs (3 or more complexes) detected by the electrocardiogram (ECG) or Holter monitoring (HM) prior to device implantation.

The study cohort (Table 1) included mainly males (84%) of working age (median age 56 (51–61) years).

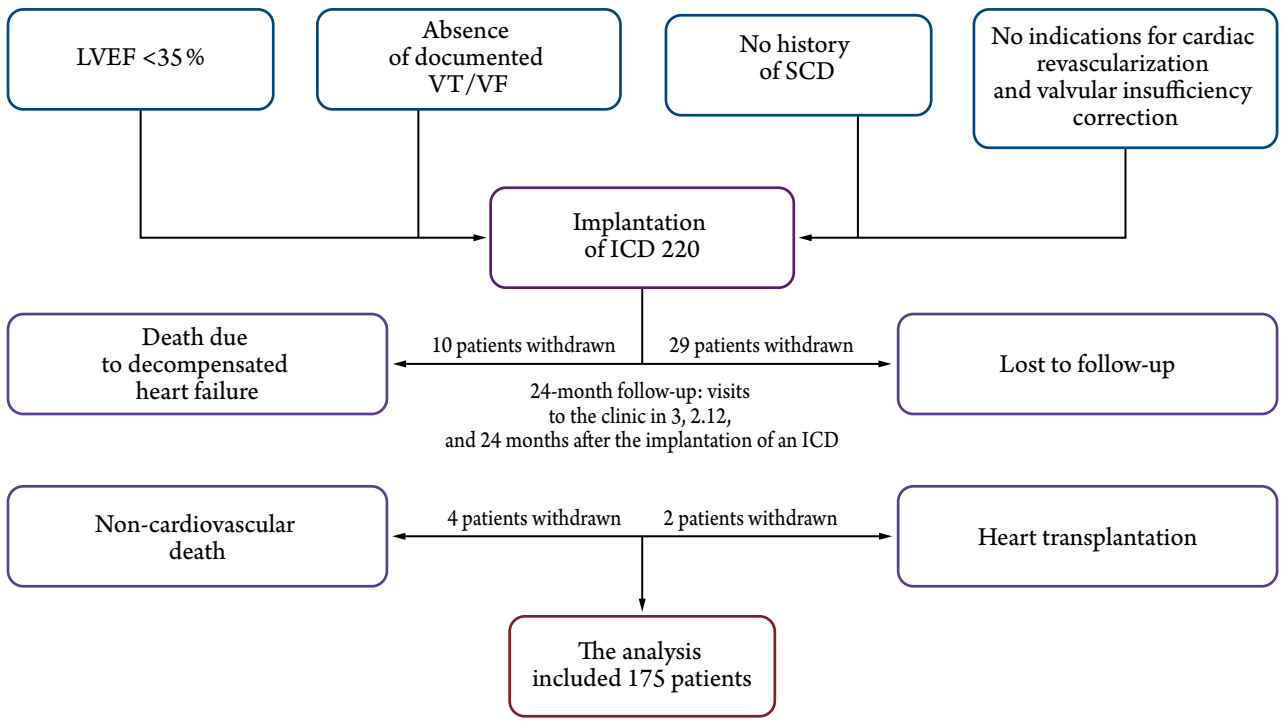
Endpoints of the study

The primary endpoint was a sustained paroxysmal VT or paroxysmal VT/VF requiring ICD implantation. Time from ICD implantation to onset of primary endpoint was also analyzed.

ICD implantation and programming

All patients included in the study had ICDs implanted as a means of primary prevention of SCD [3, 4]. Of them, 107 (61.1%) patients had severe disturbances of intraventricular conduction (QRS>150 ms), due to which cardiac resynchronization therapy (CRT) ICDs were implanted. Devices were implanted following the conventional technique described in [13].

Figure 1. Patient selection



LVEF – left ventricular ejection fraction; VT – ventricular tachyarrhythmia; VF – ventricular fibrillation; SCD – sudden cardiac death; ICD – implanted cardioverter defibrillator.

The ICDs were programmed in such a way as to minimize the likelihood of inadequate pacing and replace high-voltage shocks with anti-tachycardia stimulation. Two-zone programming (VT zone =160 bpm, VF zone =200 bpm) with the activation of supraventricular tachyarrhythmia discrimination algorithms was used to detect ventricular cardiac arrhythmias (primary endpoint).

Postoperative follow-up

Patients included in the study were followed up for two years. This period was chosen as the best possible for the preservation of safety profile when selecting patients for the ICD implantation. We are convinced of the benefits of subjecting HFrEF patients to repeated risk stratification over the following year. The low risk of developing VT is verified.

Patients were invited to visit the clinic at intervals of 3, 12, and 24 months following ICD implantation. During visits, the device was tested, and intracardiac records were analyzed. The monitoring of ICDs was remote in 88 patients. Remote notifications were set up to inform researchers of signs of possible electrode dysfunction and the registration of paroxysmal arrhythmias, including those requiring ICD therapy.

The statistical analysis of the data obtained was performed using the SPSS Statistics version 23.0 software suite. Quantitative data were described and compared depending on the nature of the distribution line, which was assessed using the Shapiro-Wilk test. If the distribution was confirmed to be normal, the data were described in terms of mean (M), standard deviation (SD) and 95% confidence interval (CI). The comparisons were performed using the Student's t-test. If the distribution was not normal, median (Me) and upper and lower quartiles [Q1; Q3] were used, with the variables being compared using the Mann-Whitney test. Nominal measures were compared using Pearson's chi-squared test. Odds ratios (OR) were used to measure the effect when the relative variables were compared. The significance of a factor was demonstrated if CI was outside the threshold of no effect equal to 1. Time to registering endpoints was evaluated using the Kaplan-Meier method, while intergroup differences were estimated using the Mantel-Cox log-rank test.

The multi-factor prognostic model was constructed to determine a two-year likelihood of Vts in HFrEF patients based on the clinical and demographic variables of interest using binary logistic regression. The independent variables were chosen by stepwise direct selection using the Wald test statistics as an exclusion criterion. The statistical significance of the model was determined using the chi-square test. The coefficient of determination (R2) served as a definiteness measure showing the part of the dispersion capable of being explained using logistic reg ression.

The significance threshold for the statistical hypotheses was 0.05.

Table 1. Clinical and demographic characteristics of the included patients (n=175)

Parameter	Value	
	n	%
Age, years*	56 [51–61]	
Male	147	84
AH	101	57,7
CAD	80	45,7
PICS	61	34,9
DCMP	89	50,9
HCM	2	1,1
RHD	3	1,7
Diabetes mellitus	33	18,9
Obesity	72	41,1
History of stroke	12	6,9
CKD	95	54,3
Surgical revascularization more than 3 months before the inclusion	75	42,8
Nonsustained VTs	9	5,1
AF (paroxysmal/persistent)	48	27,4
AF (permanent)	9	5,1
CHA_2DS_2-VASc, score	3 [2; 4]	

* The data are expressed as Me [Q1; Q3].
AH – arterial hypertension; CAD – coronary artery disease; PICS – postinfarction cardiosclerosis; DCM – dilated cardiomyopathy; HCM – hypertrophic cardiomyopathy; HRHD – chronic rheumatic heart disease; CKD – chronic kidney disease; VT – ventricular tachyarrhythmia; AF – atrial fibrillation.

Results

The primary endpoint was registered in 43 (24.4%) patients. The mean time to VT was 20.9 (95% CI 20.0–21.9) months.

The groups formed depending on the achievement of the endpoint differ significantly in the presence of nonsustained VT episodes before the ICD implantation (Table 2).

This dependence was manifested clinically as a fourfold increase in the likelihood of the arrhythmogenic scenario of SCD if the factor was detected in an HFrEF patient (OR 4.2; 95% CI 1.1–16.5; p=0.041). The dependence of the risk of the onset of the primary endpoint on a history of nonsustained VT estimated

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Table 2. Clinical and demographic characteristics of patients depending on the endpoint achievement

Indicator	Patients with VT (n=43)	Patients without VT (n=132)	p
Age, years	56 [50–61]	56 [51–61.5]	0.892
Male	37 (86.1)	110 (83.3)	0.776
AH	27 (62.8)	74 (56.1)	0.409
CAD	26 (60.5)	54 (40.9)	0.029
PICS	19 (44.2)	42 (31.8)	0.141
DCMP	11 (25.6)	78 (59.1)	<0.001
HCM	2 (4.7)	0	0.641
RHD	3 (6.9)	0	0.354
Diabetes mellitus	9 (20.9)	24 (18.2)	0.669
Obesity	17 (39.5)	55 (41.7)	0.832
History of stroke	2 (4.7)	10 (7.6)	0.733
CKD	24 (55.8)	71 (53.4)	0.243
History of surgical revascularization	24 (55.8)	51 (38.6)	0.141
Non-sustained VT	5 (11.6)	4 (3)	0.041
AF (any form)	17 (39.5)	40 (30.3)	0.252
CHA_2DS_2-VASc, score	3 [2; 4]	3 [2; 4]	0.319
CRT ICD	22 (51.2)	85 (64.4)	0.288

The data are presented as the absolute number (n) and percentage (%) of patients or Me [Q_1; Q_3]. VT – ventricular tachyarrhythmia; AH – arterial hypertension; CAD – coronary artery disease; PICS – postinfarction cardiosclerosis; DCM – dilated cardiomyopathy; HCM – hypertrophic cardiomyopathy; HRHD – chronic rheumatic heart disease; CKD – chronic kidney disease; AF – atrial fibrillation; CRT – cardiac resynchronization therapy; ICD – implantable cardioverter-defibrillator.

using the Mantel–Cox log-rank test was statistically significant (p=0.002). In the presence of previously registered nonsustained VTs, the mean time to onset of primary endpoint was 15.4 months; otherwise, it was 21.3 months (Table 3).

The comparison of the VT rates depending on the presence of CAD produced statistically significant differences (p=0.021). The likelihood of VT in the study cohort patients increased twofold in the presence of CAD (OR 2.2; 95% CI 1.1–4.5). The Kaplan–Meier analysis showed that paroxysmal VT developed earlier in patients with clinically significant CAD (Figure 2): the mean period of the manifestation was 19.7 (95% CI 18.1–21.3) months from the beginning of the follow-up in patients with HFrEF and CAD, and 22 (95% CI 21.0–23.1) months in the absence of CAD (p=0.021).

We attempted to develop a prognostic model to determine the likelihood of VTs in HFrEF patients over the next two years based on the clinical and demographic variables of interest using binary logistic regression.

The result was the following equation (1):

$$p = 1/(1+e^{-z}) \cdot 100\%$$
$$z = -1.9 + 1.8 \times X_{VT\ unst} + 0.9 \times X_{CAD} + 0.4 \times X_{AF}, \quad (1)$$

where p – two-year likelihood of VT; $X_{VT\ unst}$ – presence of nonsustained VT (0=absence, 1=presence); X_{CAD} – presence of coronary artery disease (0 = absence, 1 = presence); X_{AF} – presence of AF (0 = absence, 1 = presence); e – mathematical constant approximately equal to 2.71828.

Table 3. Survival (onset of the primary endpoint) depending on the presence of nonsustained VTs

Follow-up period, months	Nonsustained VTs present		Nonsustained VTs absent	
	n	%	n	%
6	0	0	10	6,1
12	3	40	16	9,8
18	5	70	27	16,8
24	5	70	38	25,4

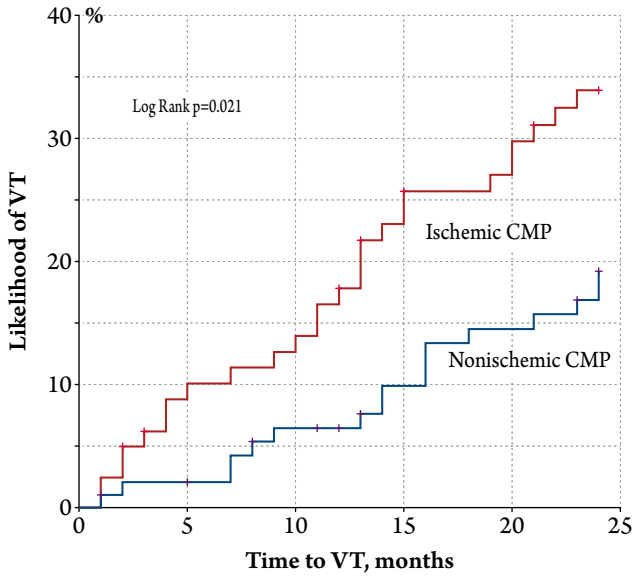
VT – ventricular tachyarrhythmia.

Based on the values of the regression coefficients, such clinical factors as the presence of nonsustained VT, CAD and AF are directly correlated with the likelihood of VT occurring over the next two years.

The resulting regression model was statistically significant (p=0.008). Based on the values of the coefficient of determination, model (1) takes into account 9.8% of the factors determining the likelihood of VT in HFrEF patients over the next two years. Diagnostic accuracy was 77.1% (sensitivity=7%, specificity=100%).

In line with the results of multivariate analysis (Table 4), the presence of nonsustained VTs increased 6.3-fold the likelihood of VT over the next two years (95% CI 1.5–26.3; p=0.012). The presence of nonsustained VTs increased 2.5-fold the likelihood

Figure 2. Kaplan-Meier curve showing the correlation between the presence of coronary artery disease and the likelihood of ventricular tachyarrhythmia in the study cohort



VT – ventricular tachyarrhythmia;
CAD – coronary artery disease; ICMP – cardiomyopathy

Table 5. Clinical and demographic characteristics of ICMP patients depending on the endpoint achievement

Indicator	Patients with VT (n=26)	Patients without VT (n=54)	p
Age, years	57.5 [52–67]	59 [54–63]	0.934
Male	25 (96.2)	49 (90.7)	0.362
AH	18 (69.2)	41 (75.9)	0.709
PICS	19 (73)	42 (77.7)	0.986
Diabetes mellitus	7 (26.9)	11 (20.4)	0.713
Obesity	11 (42.3)	24 (44.4)	0.864
History of stroke	0	4 (7.4)	0.288
CKD	14 (63.6)	35 (67.3)	0.974
History of surgical revascularization	24 (92.3)	51 (94.4)	0.428
Nonsustained VTs	2 (7.7)	0	0.133
AF (any form)	9 (34.6)	22 (40.7)	0.614
CHA_2DS_2-VASc, score	3 [3; 4]	3 [3; 4]	0.544

The data are presented as the absolute number (n) and percentage (%) of patients or Me [Q1; Q3].
ICMP – ischemic cardiomyopathy; VT – ventricular tachyarrhythmia; AH – arterial hypertension; PICS – postinfarction cardiosclerosis; CKD – chronic kidney disease; AF – atrial fibrillation.

Table 4. Correlation of the factors of interest and primary endpoint

Factor	OR	95% CI	p
Univariate analysis			
Age	1	0,97–1,1	0,514
Male	0,8	0,3–2	0,768
CAD	2,2	1,1–4,5	0,021
PICS	1,7	0,8–3,4	0,144
AH	1,3	0,7–2,7	0,438
Diabetes mellitus	1,3	0,5–2,97	0,772
Obesity	0,9	0,47–1,9	0,874
History of stroke	0,6	0,13–2,8	0,733
CKD	1,1	0,54–2,2	0,817
History of surgical revascularization	1,7	0,86–3,4	0,144
Nonsustained VTs	4,2	1,1–16,5	0,041
AF (any form)	1,5	0,74–3,1	0,262
CHA_2DS_2-VASc, score	1,2	0,89–1,6	0,216
Multivariate analysis			
CAD	2,5	1,2–5,1	0,018
Nonsustained VTs	6,3	1,5–26,3	0,012

OR – odds ratio; CI – confidence interval; CAD – coronary artery disease; PICS – postinfarction cardiosclerosis; AH – arterial hypertension; CKD – chronic kidney disease; VT – ventricular tachyarrhythmia; AF – atrial fibrillation.

Table 6. Clinical and demographic characteristics of NICMP patients depending on the endpoint achievement

Indicator	Patients with VT (n=17)	Patients without VT (n=78)	p
Age, years	52 [50–58]	55 [48–59]	0.733
Male	12 (70.6)	60 (76.9)	0.552
AH	9 (52.9)	33 (42.3)	0.589
Diabetes mellitus	2 (11.8)	12 (15.4)	0.988
Obesity	6 (35.3)	30 (38.5)	0.991
History of stroke	2 (11.8)	6 (7.7)	0.634
CKD	10 (62.5)	36 (51.4)	0.603
Nonsustained VTs	3 (17.6)	4 (5.1)	0.114
AF (any form)	8 (47.1)	18 (23.1)	0.047
CHA_2DS_2-VASc, score	2 [1; 4]	2 [1; 3]	0.879

The data are presented as the absolute number (n) and percentage (%) of patients or Me [Q1; Q3].
NICMP – non-ischemic cardiomyopathy; VT – ventricular tachyarrhythmia; AH – arterial hypertension; CKD – chronic kidney disease; VT – ventricular tachyarrhythmia; AF – atrial fibrillation.

of VT over the next two years (95% CI 1.2–5.1; p=0.018).

Given the correlation between the presence of CAD and VT, we analyzed the clinical and demographic variables of interest and the incidence of the events in subgroups of patients with ischemic cardiomyopathy (ICMP) and non-ischemic cardiomyopathy (NICMP). These data are presented in Table 5 and Table 6. The differences in the incidence of VT depending on the presence of any

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AF were statistically significant in NICMP patients (p=0.047). The presence of this type of arrhythmia with underlying NICMP and low LVEF increased the likelihood of the arrhythmogenic scenario of SCD almost threefold (OR 2.97; 95% CI 1.02–8.8). In the multivariate analysis, OR increased to 3.5 (95% CI 1.1–10.9; p=0.032).

Discussion

Nonsustained VT and the likelihood of clinically significant VTs in the future

According to our data, fatal HA VAs were both more frequent (fourfold) and earlier in HFrEF patients with nonsustained Vas following the implantation of ICDs (15.4 vs. 21.3 months, respectively).

Previous publications showed that the presence of nonsustained VT in the echocardiographic records was associated in patients with ICDs implanted as primary prevention of SCD with increased mortality (2.4-fold), and the risk of adequete pacing (threefold) [14]. Some authors emphasized that nonsustained VTs have prognostic value in patients with CHF and preserved LVEF [14].

According to Zecchin et al. [15], the presence of nonsustained VT does not contribute to the prediction of the fatal VA likelihood in patients with NICMP and LVEF ≤5%: this information only becomes useful when LVEF > 35% (OR 5.3; 95% CI 1.6–17.9).

Hashimoto et al. [16] concluded in their study that nonsustained VT registered in patients with myocardial infarction (MI) had an independent prognostic value for the future outcomes of arrhythmia (OR 3.6; 95% CI 1.6–11.2; p=0.027). When such arrhythmia is registered, and late potentials are detected on the ECG, the risk of VA is almost fourfold (OR 14.1, 95% CI 3.4–58.9; p<0.0001) [16]. Similar conclusions were drawn for NICMP patients [12].

Manifestion of VT episodes can comprise evidence of high activity of the ectopic center and the presence of the re-entry tachycardia substrate. Regardless of the origin of systolic dysfunction, ICD therapy is indicated in the event of sustained VT (class I, level A) under the available recommendations for HFrEF patients [4]. When nonsustained paroxysmal VTs are registered, management is usually limited by antiarrhythmic therapy, while the need for the implantation is estimated only by LVEF (≤40% with a history of MI or ≤35% in other cases) [2]. Our results raise the question once again whether it is necessary to review approaches to stratifying the risk of arrhythmias and complications in patients with HFrEF. A history of nonsustained VTs may be an important indicator of a high likelihood of fatal VAs occurring in the future.

CAD and the likelihood of clinically significant VTs in the future

The study results provide evidence of differences in the incidence of VT in patients with ICMP and NICMP, which is also confirmed by the literature [8]. It obvious that such differences are due to the different pathophysiological mechanisms inducing VAs in these groups of patients [17].

The SCD scenario is realized in patients with ICMP in the presence of peri-infarct zones bordering the myocardial scar. The morphological heterogeneity of the myocardium is due to the fact that some muscle fibers are still oxygenated despite the coronary disease of the arteries responsible for the blood supply to this part of the myocardium [18]. These clusters of viable cardiomyocytes within the scar cause electrical anisotropy with electrical conduction blocks. As a result, the ideal conditions are created for re-entry VT [19].

It is often impossible to clearly visualize the scar in patients with NICMP, since numerous small-sized areas of myocardial fibrosis are detected [20]. For this reason, the re-entry mechanism is responsible for only 40% of VAs, while a leading cause of arrhythmogenesis is the increased trigger activity (early or delayed postdepolarization, increased automatism) [21].

These data suggest that patients with ischemic HFrEF have a more significant arrhythmogenic potential, which should be taken into account in the SCD risk stratification. However, the study design did not imply an analysis of echocardiograms (both standard and using speckle tracking), gadolinium-enhanced magnetic resonance imaging (MRI) of the heart, or other examinations capable of identifying a possible anatomical substrate of VT. The groups with VTs and without the onset of the primary endpoint were comparable by a single clinical indicator that provides such information, i.e., the presence of postinfarction cardiosclerosis (Table 2).

AF and the likelihood of clinically significant VTs in the future

Literature data indicate a close correlation between arrhythmogenic SCD and AF [22, 23]. The high ventricular rate during the episodes of tachysystolic AF is known to reduce myocardial refractivity and provoke VT [24]. Irregular rhythm in AF with the preserved fast atrioventricular conduction may cause proarrhythmic conditions essentially similar to those in the programmed ventricular stimulation [25].

Although we failed to establish a correlation between AF and VT rates in all subjects with HFrEF, our findings show that the risk of fatal VAs in patients with non-ischemic HFrEF increases almost threefold (OR 2.97; 95% CI 1.02–8.8) in AF of any form.

There can be little doubt that the main pathogenetic substrate of VAs in patients with NICMP is diffuse myocardial fibrosis [26, 27]. A complex chain of cellular remodeling in atrial fibrosis outcome also underlies AF [28]. Some researchers also believe that AF can initiate collagen synthesis to act as an independent factor of the progression of ventricular fibrosis [29, 30]. Ling et al. [31] performed MRI T1 mapping in 90 patients (without AF – 23, paroxysmal AF – 40, persistent AF – 27) to show a direct correlation between increasing post enhancement time T1 (a sign of myocardial fibrosis) and the presence of AF; moreover, LV fibrosis was detected in patients with AF [31]. Thus, the progression of myocardial fibrosis can manifest in patients NICMP as AF and VT [32, 33].

CHA_2DS_2VASc and the likelihood of clinically significant VTs in the future

The CHA_2DS_2VASc scale, which was initially developed to assess the risk of stroke in patients with non-rheumatic AF, attracts the attention of researchers as an indicator of cerebrovascular risk, including cardiovascular death [34]. It should be noted that the prognostic value of this scale is asserted to apply to all patients with or without AF [35].

In this context, the Taiwanese register study provokes interest by demonstrating that an increase in the CHA_2DS_2VASc score by one point increases 1.21-fold the likelihood of fatal VAs (95% CI 1.2–1.22) [36].

According to the MADIT-CRT (Multicenter Automatic Defibrillator Implantation Trial With Cardiac Resynchronization Therapy) study, which included 1,804 patients with HFrEF, high risk as assessed by the CHA_2DS_2VASc score (>5) is associated with increased mortality (OR 1.92, $p<0.001$), including due to decompensated CHF (OR 1.6; $p<0.001$), but with a low risk of developing VAs (OR 0.64; $p=0.001$) and pacing (HR 0.51, $p<0.001$) [37].

Based on the data presented, the prospect of using the CHA_2DS_2VASc scale for the risk stratification of arrhythmias and complications in patients with HFrEF appears to be highly promising. The high severity of the disorder and potentially more adverse course of CHF is demonstrated by the 106 (60.6%) patients in our study having $CHA_2DS_2VASc \geq 3$. However, no evidence of a correlation between CHA_2DS_2VASc scores and the incidence of VTs was obtained.

Limitations

Although the study included relatively few patients with HFrEF (n=175), this number was sufficient to detect statistically significant correlations between the primary endpoint and clinical factors of interest. However, a more numerous cohort could undoubtedly provide additional information and enhance the statistical reliability of several correlations.

The primary endpoint was evaluated based on the scanning of ICDs. The identification of VT episodes was restricted by a lower rate of ventricular events detected by the device (VA less than 160 per minute for all patients). For this reason, it was not possible to diagnose episodes of VT with a lower rate.

Although 61.1% of subjects had CRT ICDs implanted, the nature of response to CRT was not investigated in this study. Despite the approximately equal distribution of devices in the groups depending on the onset of the primary endpoint, CRT could potentially modify the primary SCD substrate in individual patients.

Conclusions

1. All patients experiencing chronic heart failure with reduced left ventricular ejection fraction are at potential risk of sudden cardiac death. The incidence of ventricular tachyarrhythmias was 24.4% over the following two years.
2. Nonsustained paroxysmal ventricular tachyarrhythmias in patients with chronic heart failure with reduced left ventricular ejection fraction, as registered by electrocardiogram or Holter monitoring, is 6.3 times higher than the likelihood of life-threatening ventricular arrhythmias. This factor may evidence a high arrhythmic risk requiring the implantation of a cardioverter-defibrillator.
3. The origin of heart failure can determine the likelihood of fatal ventricular outcomes in the near future. Ischemic chronic heart failure with reduced left ventricular ejection fraction increases the risk of ventricular tachyarrhythmias over the next two years by 2.5 times.
4. Atrial fibrillation in patients having non-ischemic chronic heart failure with reduced left ventricular ejection fraction increases threefold the risk of ventricular tachyarrhythmias over the following two years, which should be taken into account in the stratification of the risk of sudden cardiac death in this patient cohort.

No conflict of interest is reported.

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