Predictors of ventricular tachyarrhythmia in patients with implantable cardioverter-defibrillator and non-ischemic systolic heart failure

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ABSTRACT

Background: The benefit derived from implantable cardioverter-defibrillators (ICD) in subjects with non-ischemic systolic HF (NICM) is less well-established.

Aim: The study aimed to determine the incidence, predictors, and prognostic impact of ventricular arrhythmias in patients with ICD and NICM.

Methods: The study sample included 377 consecutive patients with ICD or cardiac resynchronization cardioverter-defibrillators (CRT-D, 74% of patients) and NICM implanted and monitored remotely in a university hospital.

Results: During the median (interquartile range [IQR]) follow-up of 1645 (960–2675) days, sustained ventricular arrhythmia occurred in 92 patients (24.4%). Of those, ventricular fibrillation (VF), ventricular tachycardia (VT), and both VT and VF occurred in 10 (10.9%), 72 (78.3%), and 10 (10.9%) patients, respectively. Patients with *vs.* those without ventricular arrhythmia differed concerning sex, left ventricular end-diastolic diameter (LVEDD), left ventricular end-systolic diameter (LVESD), left ventricular ejection fraction (LVEF), post-inflammatory etiology, atrial fibrillation/flutter occurrence, and supraventricular arrhythmia (SVT) other than AF/AFL during follow-up. In multivariable Cox regression, LVEDD (hazard ratio [HR], 1.05; 95% confidence interval [CI], 1.003–1.09; $P = 0.03$), AF/AFL (HR, 1.86; 95% CI, 1.21–2.85; $P = 0.004$), and SVT (HR, 1.77; 95% CI, 1.10–2.87; $P = 0.02$) were independent predictors of sustained VT, while AF/AFL (HR, 1.65; 95% CI, 1.07–2.56; $P = 0.02$) was independent predictor of VF. All-cause mortality in patients with VT/VF was significantly higher than in subjects without sustained ventricular arrhythmias (35.9% vs. 22.4%; $P = 0.01$).

Conclusions: Ventricular arrhythmia occurred in every fourth patient with NICM and ICD during 4.5 years of observation and was associated with significantly worse prognosis than in subjects free of VT/VF. Higher LVEDD, atrial fibrillation/atrial flutter, and supraventricular tachycardia flag patients at risk of ventricular arrhythmia.

Key words: appropriate therapy, heart failure, implantable cardioverter-defibrillator, predictors, ventricular arrhythmia

INTRODUCTION

Implantable cardioverter-defibrillators (ICD) reduce the risk of sudden cardiac death (SCD) and improve prognosis in patients with heart failure (HF) and decreased left ventricular ejection fraction (LVEF). However, though the benefit has been demonstrated for patients with ischemic HF [1], the value of ICD in subjects with non-ischemic systolic HF (NICM) is less well-established. Moreover, there is limited evidence on which NICM patients would benefit most from receiving an ICD. Retrospective

WHAT'S NEW?

As opposed to patients with ischemic heart failure (HF), the benefit derived from implantable cardioverter-defibrillators (ICD) in subjects with non-ischemic systolic HF (NICM) is less well-established. We report that the incidence of sustained ventricular arrhythmias in NICM patients reaches 24.4% during 4.5 years of observation (54.1 per 1000 person-years). Left ventricular dimension, atrial fibrillation/atrial flutter, and supraventricular tachycardia during follow-up are strong and independent risk factors for ventricular arrhythmia in NICM subjects. Occurrence of ventricular arrhythmia is associated with significantly worse prognosis, with fatality rates exceeding 36%.

and observational studies showed that the ICD improves prognosis in subjects with non-ischemic cardiomyopathy [2–4]. Nevertheless, this was not confirmed in randomized controlled trials, and all-cause mortality did not differ between the ICD and control group in the DANISH trial, with a 50% reduction in the risk of SCD [5]. On the other hand, SCD rates in optimally pharmacologically treated patients are low: the SCD rate was less than 2% per year in the control group in the DANISH trial [5]. It might be that only patients with a sufficiently high risk of SCD and a relatively low risk of death from other causes benefit from an ICD. On the contrary, new data imply that, currently, optimally treated patients (i.e., with sacubitril/valsartan, which reduces SCD rates regardless of HF reason) also benefit from ICD implantation [4].

Thus, our study aimed to determine the incidence and predictors of ventricular arrhythmia in patients with ICD and NICM and to assess mortality in subjects with and without ventricular arrhythmias.

METHODS

Study population

All consecutive patients with NICM implanted with ICD and monitored remotely between February 2010 and December 2016 in a tertiary care university hospital in a densely inhabited, urban region of Poland were included in the prospective single-center registry. All patients met the criteria for ICD implantation in primary or secondary prevention of SCD, in line with the current European Society of Cardiology (ESC) guidelines. Each patient signed informed consent to undergo the procedure. Implantations of ICDs and cardiac resynchronization devices with defibrillator (CRT-D) were performed according to the current standards. The echocardiographic examinations were performed according to the standard protocol before device implantation. Data derived from this examination were included in the analysis. The study was conducted in compliance with the Declaration of Helsinki.

Data collection, follow-up, and classification of arrhythmic events

Patients were followed up one week, one month after the implantation procedure, and every six months afterward until July 2017. All patients were assessed during scheduled and unscheduled visits; data were retrieved from hospital records, outpatient notes, telephone calls, insurer's records, and death certificates obtained directly from patient records or relatives.

After signing informed consent and being instructed on how the remote monitoring works, all patients received a portable wireless transmitter that transmits data via the GSM network to the central server. Data retrieved from the devices were available online to medical staff after logging online to the Biotronik Home Monitoring, Medtronic CareLink, or St. Jude Medical Merlin.net remote monitoring systems, as appropriate. The transmissions were received routinely as electively scheduled and emergency reports in the case of pre-defined device alerts.

Implanted ICD and CRT-D devices detected ventricular tachycardia (VT) and ventricular fibrillation (VF) episodes if the ventricular rate was higher than the programmed value and the episode persisted longer than the minimum programmed count. The discriminators of ventricular arrhythmias were programmed according to the manufacturer's recommendations and, if needed, were reprogrammed individually according to the patient's needs (e.g. in cases of inappropriate ICD therapy due to supraventricular arrhythmia).

Two experienced cardiologists assessed every recorded episode based on intracardiac electrograms (EGMs).

Statistical analysis

The continuous parameters were expressed as medians (interquartile range [IQR]), whereas categorical variables were expressed as numbers and percentages. The groups were compared using the Chi-square, or Mann-Whitney U tests, as appropriate. Survival was analyzed using the Kaplan-Meier estimator and the log-rank test. Independent risk factors for arrhythmias and mortality were analyzed using the proportional hazards method (Cox's regression). The multivariate model was constructed using baseline confounders that differentiated study groups with a *P*-value of <0.05. Results were expressed as hazard ratio (HR) with 95 percent confidence intervals (95% CI).

A *P*-value of less than 0.05 was considered statistically significant. All statistical analyses were performed using the Statistica software package (version 6.0, StatSoft Inc., Tulsa, OK, US, and version 10.0).

Table 1. Baseline characteristics of patients with and without sustained ventricular arrhythmias

	Whole population (n = 377)	Patients without VA (n = 285)	Patients with VA (n = 92)	*P*-value[a]
Age, years	60 (52–67)	60 (50–67)	60 (54–66)	0.85
Male sex	267 (71)	193 (68)	74 (80)	0.02
NYHA class	3 (2–3)	3 (2–3)	3 (2–3)	0.98
LVEF, %	27 (21–34)	28 (22–34)	25 (20–31)	0.048
LVESD, mm	53 (44–62)	52 (44–62)	56 (47–64)	0.03
LVEDD, mm	65 (58–72)	64 (57–71)	68 (60–76)	0.006
Primary prevention of SCD	306 (81)	235 (82)	71 (77)	0.26
Secondary prevention of SCD	71 (19)	50 (18)	21 (23)	0.26
Dilatative cardiomyopathy	253 (67)	189 (66)	64 (70)	0.56
Hypertrophic cardiomyopathy	43 (11)	38 (13)	6 (6)	0.08
Inflammatory cardiomyopathy	48 (13)	32 (11)	14 (15)	0.31
Non-compaction cardiomyopathy	26 (7)	20 (7)	7 (8)	0.85
Other (ARVD, toxic, congenital heart defect)	7 (2)	6 (7)	1 (1)	0.53
ICD	99 (26)	75 (26)	24 (26)	0.97
CRT-D	278 (74)	210 (74)	68 (74)	0.97
Diabetes	79 (21)	56 (20)	23 (25)	0.27
Creatinine, µmol/l	83 (70–107)	86 (70–107)	81 (69–109)	0.89
Hypertension	170 (45)	126 (44)	44 (48)	0.54
AF/AFL (paroxysmal, persistent, permanent)	171 (45)	115 (40)	56 (61)	<0.001
AF permanent	75 (19.9)	53 (18.6)	22 (23.9)	0.27
Supraventricular tachycardia during follow-up	69 (18)	45 (16)	24 (26)	0.03
Severe MR	27 (7)	17 (6)	10 (11)	0.11
Medications at discharge				
β-blocker	358 (95)	268 (94)	90 (98)	0.15
ACEI/ARB	326 (86)	242 (85)	84 (91)	0.12
Loop diuretics	259 (69)	186 (65)	73 (79)	0.01
Aldosterone antagonist	290 (77)	217 (76)	73 (79)	0.53

Continuous variables are presented as medians (IQR) and categorical variables as numbers (percentages)

[a]*P*-value for comparison between patients with and without VA

Abbreviations: ACEI, angiotensin-converting-enzyme inhibitors; AF, atrial fibrillation; AFL, atrial flutter; ARB, angiotensin receptor blockers; ARVD, arrhythmogenic ventricular dysplasia; CRT-D, cardiac resynchronization therapy with defibrillator; ICD, implantable cardioverter-defibrillator; LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic diameter; MR, mitral regurgitation; NYHA, New York Heart Association; SCD, sudden cardiac death; VA, ventricular arrhythmia

RESULTS

Study population

The study population comprised 377 consecutive NICM patients with ICD/CRT-D. The median (IQR) age of patients was 60 (52–67) years; 71% were male, and the median left ventricular ejection fraction was 27 % (21%–34%).

During the median follow-up of 1645 (960–2675) days, ventricular arrhythmia occurred in 92 patients (24.4%). Of those, ventricular fibrillation (VF), ventricular tachycardia (VT), and both VT and VF occurred in 10 (10.9%), 72 (78.3%), and 10 (10.9%) patients, respectively. Patients with versus those without ventricular arrhythmia differed with respect to sex (80% vs. 68% male; $P = 0.02$), left ventricular end-diastolic diameter (LVEDD, median of 68 [60–76] mm vs. 64 [57–71] mm; $P = 0.006$), left ventricular end-systolic diameter (LVESD, 56 [47–64] mm vs. 52 [44–62] mm; $P = 0.006$), left ventricular ejection fraction (LVEF, 25% [20%–31%] vs. 28% [22%–34%]; $P = 0.048$), atrial fibrillation/flutter occurrence (AF/AFL, 61% vs. 40%, $P < 0.001$), and supraventricular arrhythmia (SVT) other than AF/AFL during follow-up (26% vs. 16%; $P = 0.03$). No differences were observed in age, NYHA class, primary vs. secondary SCD prevention, mitral regurgitation, or common comorbidities, including diabetes and chronic renal disease (Table 1).

There were 74% (n = 278) of patients with CRT-D and 26% (n = 99) of patients with ICD. Of these patients in the group of CRT-D and ICD, 68 (24.5%) and 24 (24.2%) subjects had ventricular arrhythmias, respectively.

There were 23% of patients (n = 21/91) with secondary prevention of SCD who experienced ventricular arrhythmia during follow-up in our study, and 18% of subjects (n = 50/285) with secondary prevention of SCD but without arrhythmia ($P = 0.26$). In the group of patients with secondary prevention of SCD, 29.6% experienced ventricular arrhythmia, whereas in the group with primary prevention, the percentage of subjects with arrhythmias during follow-up was 23.2%.

In the whole population, patients alive versus deceased did differ with respect to NYHA class ($P = 0.001$), left ventricular end-diastolic diameter (LVEDD, median of 64 [57–71] mm vs. 69 [60–78] mm; $P = 0.006$), left ventricular end-systolic diameter (LVESD, 51 [42–61] mm vs. 58 [49–66] mm; $P < 0.001$), left ventricular ejection fraction (LVEF, 28% [23%–36%] vs. 23% [20%–29%];

Table 2. Baseline characteristics of the whole study population and patients with ventricular arrhythmias in relation to vital status

	Whole population (n = 377)		*P*–value[a]	Patients with ventricular arrhythmias (n = 92)		*P*-value[a]
Patients	Alive (n = 280) 74.3	Deceased (n = 97) 25.7		Alive (n = 59) 64.1	Deceased (n = 33) 35.9	
	58 (50–66)	62 (54–69)	0.06	58 (53–66)	62 (57–66)	0.53
Male sex	199 (71.1)	68 (70.1)	0.86	46 (77.9)	28 (84.8)	0.42
NYHA class	3 (2–3)	3 (2–3)	0.001	3 (2–3)	3 (2–3)	0.02
LVEF, %	28 (23–36)	23 (20–29)	<0.001	27 (23–36)	20 (19–27)	0.002
LVESD before CRT-D/ICD, mm	51 (42–61)	58 (49–66)	<0.001	53 (42–61)	60 (55–70)	<0.001
LVEDD before CRT/ICD, mm	64 (57–71)	69 (60–78)	<0.001	67 (59–72)	72 (60–81)	0.03
Primary prevention of SCD	229 (81.8)	77 (79.4)	0.60	44 (74.6)	27 (81.8)	0.43
Secondary prevention of SCD	51 (18.2)	20 (20.6)	0.60	15 (25.4)	6 (18.2)	0.43
Dilatative cardiomyopathy	181 (64.6)	72 (74.2)	0.08	43 (72.9)	25 (75.8)	0.76
Hypertrophic cardiomyopathy	36 (12.9)	7 (7.2)	0.13	5 (8.5)	1 (3.0)	0.31
Inflammatory cardiomyopathy	39 (13.9)	9 (9.3)	0.24	13 (22)	4 (12.1)	0.24
Non-compaction cardiomyopathy	21 (7.5)	5 (5.2)	0.43	6 (10.2)	1 (3)	0.22
ICD	89 (31.8)	10 (10.3)	<0.001	20 (33.9)	4 (12.1)	0.02
CRT-D	191 (68.2)	87 (89.7)	<0.001	39 (66.1)	29 (87.9)	0.02
Diabetes	52 (18.6)	27 (27.8)	0.05	14 (23.7)	9 (27.3)	0.71
Creatinine, µmol/l	81 (69–103)	94 (78–124)	<0.001	81 (67–108)	83 (73–123)	0.23
Hypertension	123 (43.9)	47 (48.5)	0.44	29 (49.2)	15 (45.5)	0.73
AF/AFL	112 (40)	59 (60.8)	<0.001	33 (55.9)	23 (69.7)	0.19
Supraventricular tachycardia during follow-up	54 (19.3)	15 (15.5)	0.40	15 (25.4)	9 (27.3)	0.85
VA during follow-up	59 (21.1)	33 (34)	0.01	NA	NA	NA
Severe MR	18 (6.4)	9 (9.3)	0.35	7 (11.9)	3 (9.1)	0.68
Medications at discharge						
β-blocker	265 (94.6)	93 (95.9)	0.63	58 (98.3)	32 (96.9)	0.67
ACEI/ARB	237 (84.6)	89 (91.8)	0.08	53 (89.8)	31 (93.9)	0.50
Loop diuretics	171 (61.1)	88 (90.7)	<0.001	43 (72.9)	30 (90.9)	0.04
Aldosterone antagonist	207 (73.9)	83 (85.6)	0.02	46 (77.9)	27 (81.8)	0.66

Continuous variables are presented as medians (IQR), categorical variables as numbers (percentages)

[a]*P*-value for comparison between patients with and without VA

Abbreviations: see Table 1

P <0.001), CRT-D (68.2% vs. 89.7%; *P* <0.001), creatinine level (81 [69–103] µmol/l vs. 94 [78–124] µmol/l; *P* <0.001), AF/AFL during follow-up (40% vs. 59%; *P* <0.001) and VT/VF during follow-up (21.1% vs. 34%; *P* = 0.01). Baseline characteristics of the whole study population and patients with ventricular arrhythmias in relation to vital status have been presented in Table 2.

Predictors of ventricular arrhythmias and death

In multivariable Cox regression analysis, LVEDD (HR, 1.05; 95% CI, 1.003–1.09; *P* = 0.03), AF/AFL (HR, 1.86; 95% CI, 1.21–2.85; *P* = 0.004), and SVT (HR, 1.77; 95% CI, 1.10–2.87; *P* = 0.02) were independent predictors of sustained VT in patients with ICD and NICM (Table 3). The only independent predictor of VF was AF/AFL (HR, 1.65; 95% CI, 1.07–2.56; *P* = 0.02).

The multivariable analysis model for subjects with primary prevention of sudden cardiac death showed LVEDD (HR, 1.06; 95% CI, 1.01–1.11; *P* = 0.01), AF/AFL (HR, 2.26; 95% CI, 1.37–3.72; *P* = 0.001), and SVT (HR, 2.10; 95% CI, 1.18–3.73; *P* = 0.01) as independent predictors of VT in patients with NICM and ICD.

The multivariable analysis model for mortality prediction in the whole population showed LVEF (HR, 0.96; 95% CI, 0.93–0.99; *P* = 0.04), creatinine at baseline (HR, 1.01; 95% CI, 1.004–1.02; *P* <0.001), and AF/AFL during follow-up (HR, 1.56; 95% CI, 1.03–2.37; *P* = 0.04) as independent predictors of death in patients with NICM and ICD (Table 4).

Mortality and device-related adverse events

During the follow-up, 97 patients (25.7%) died: 33 subjects with ventricular arrhythmias and 64 patients in the group without ventricular arrhythmias. All-cause mortality in patients with VT/VF was significantly higher than in subjects without sustained ventricular arrhythmias (35.9% vs. 22.4%, *P* = 0.01). The Kaplan-Meier curves of survival in patients with and without ventricular arrhythmias are shown in Figure 1.

The incidence of cardiac device-related infective endocarditis (CDRIE) was 3.7% (n = 14). However, a total of 61 leads in 47 patients (12.5%) were replaced for non-infectious reasons (dislocation, dysfunction, fracture, etc.). No differences in the incidence of CDRIE and lead malfunctions were observed between patients with and without ventricular arrhythmias.

Table 3. Multivariable Cox regression models for prediction of ventricular arrhythmias

Predictors of ventricular arrhythmias — VT		
Variable	**HR (95% CI)**	***P*-value**
Male sex	1.39 (0.78–2.50)	0.26
AF/AFL	1.86 (1.21–2.85)	0.004
SVT	1.77 (1.10–2.87)	0.02
LVEF at baseline	0.99 (0.96–1.01)	0.34
LVEDD at baseline	1.05 (1.003–1.09)	0.03
LVESD at baseline	0.97 (0.93–1.003)	0.07
Predictors of ventricular arrhythmias — VF		
Variable	**HR (95% CI)**	***P*-value**
Male sex	1.46 (0.85–2.52)	0.17
AF/AFL	1.65 (1.07–2.56)	0.02
SVT	1.40 (0.87–2.27)	0.17
LVEF at baseline	1.005 (0.98–1.03)	0.71
LVEDD at baseline	1.03 (0.99–1.08)	0.13
LVESD at baseline	0.99 (0.95–1.03)	0.49

Abbreviations: HR, hazard ratio; LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic diameter; SVT, supraventricular tachycardia; VF, ventricular fibrillation; VT, ventricular tachycardia; other —see Table 1

Table 4. Multivariable Cox regression model for mortality prediction in the whole population

Variable	HR (95% CI)	*P*-value
CRT-D	0.87 (0.42–1.83)	0.72
NYHA class	1.03 (0.69–1.54)	0.89
LVEF at baseline	0.96 (0.93–0.99)	0.04
LVEDD at baseline	0.98 (0.94–1.06)	0.44
LVESD at baseline	1.02 (0.98–1.06)	0.44
Creatinine at baseline	1.01 (1.004–1.02)	<0.001
AF/AFL	1.56 (1.03–2.37)	0.04
VA	0.84 (0.29–2.47)	0.75

Abbreviations: see Tables 1 and 3

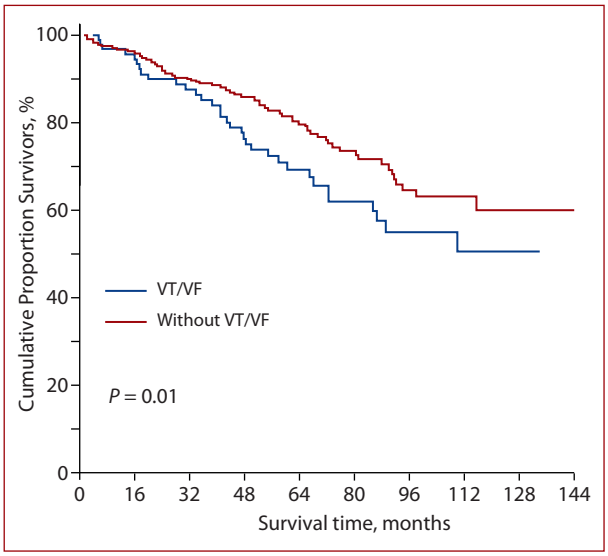

Figure 1. Kaplan-Meier curves of survival in patients with vs. without VT/VF

Abbreviations: VF, ventricular fibrillation; VT, ventricular tachycardia

DISCUSSION

The main findings of our study are as follows: (1) the incidence of ventricular arrhythmias in NICM patients reaches 24.4% during 4.5 years of observation (54.1 per 1000 person-years); (2) left ventricular dimension, atrial fibrillation/atrial flutter, and supraventricular tachycardia during follow-up are strong and independent risk factors for ventricular arrhythmia in this group; (3) occurrence of ventricular arrhythmia is associated with significantly worse prognosis, with fatality-rates exceeding 36%.

The value of implanting ICD in patients with NICM is still being discussed after the DANISH trial. However, during long-term observation, patients aged ≤70 years had a lower long-term incidence of all-cause mortality and cardiovascular death in the ICD group, compared with the control group [5, 6]. Lower SCD incidence in the ICD group was observed in the overall population in the extended DANISH follow-up [6]. Similarly, meta-analyses that included the results of the DANISH trial showed a significant mortality reduction in subjects with ICD implanted for primary SCD prevention [7–10]. It has been shown that the modern pharmacological treatment of HF improves patient prognosis by reducing the incidence of ventricular arrhythmias and the risk of SCD [11]. Therefore, identifying patients at sufficiently high risk of ventricular arrhythmias and low risk of death from other causes who will ultimately benefit from ICD implantation remains an issue in cardiology. Regardless of the reasons, presently, the risk stratification for ICD implantation is continuously and predominantly based on LVEF. This strategy may lead to overtreatment of patients from the primary SCD prevention group, as most of them presumably will never need an ICD [12]. This issue is being currently investigated in patients with non-ischemic HF and subjects with prior myocardial infarction [13].

In our study, the incidence of ventricular arrhythmia in NICM patients reached 24.4% during 4.5 years of observation, resulting in an incidence of 54.1 per 1000 person-years. In the DEFINITE trial, at least one appropriate device intervention was observed in 18% of subjects during a mean follow-up of 2.5 years [2]. In the DAI-PP study, almost 22% of patients with non-ischemic cardiomyopathy experienced at least one episode of ventricular tachyarrhythmia requiring ICD intervention during a mean follow-up of 2.9 ± 2.1 years [14]. It seems that almost a quarter of patients experience ventricular arrhythmia with appropriate ICD intervention within approximately 3–4 years of follow-up. Notably, no significant differences were reported in NICM and ischemic cardiomyopathy (ICM) subjects regarding appropriate device interventions [14, 15].

Beyond considering NYHA class and LVEF, better identification of the subgroup of NICM patients who would benefit from an ICD is challenging, at least partly because non-ischemic cardiomyopathy includes heterogeneous etiologies. The majority of studies that aimed to identify

independent risk factors of SCD and all-cause mortality in ICD patients to define the target ICD population (that is, those who would benefit from ICD implantation) included patients with both ischemic and non-ischemic HF [16–18]. Our study included only patients with NICM and identified left ventricular dimensions, atrial fibrillation/atrial flutter, and supraventricular tachycardia as strong and independent risk factors for ventricular arrhythmia.

Currently, LVEF is an essential parameter to assess the risk of ventricular arrhythmias and qualify patients for ICD implantation. Search for other echocardiographic parameters is still ongoing. Some risk models try to integrate further information, such as CMR-derived late gadolinium enhancement (LGE) if available [19], or novel echocardiographic techniques, such as global longitudinal strain tissue characterization by echocardiography or CMR. Nevertheless, obtaining these parameters is time-consuming and expensive, and until now, their usefulness has been assessed in the diagnosis and prediction of outcomes in HF patients [20, 21] but not confirmed in SCD. Our analysis points out that simple parameters, such as left ventricular dimensions, are reliable indicators of adverse remodeling and, thus, of an increased risk of arrhythmia.

Atrial fibrillation or flutter is another independent parameter associated with increased risk of ventricular arrhythmias. AF/AFL in our study increased the probability of VT by 1.87-fold and VF by 1.65-fold. Previous studies in patients with ischemic and non-ischemic heart failure demonstrated that atrial arrhythmia is a risk factor for all-cause mortality, non-sudden cardiovascular death, and HF decompensation. Recently published data showed similar outcomes — the risk of VT/VF in the group of patients with AF was 1.3–1.7-fold higher than in subjects with sinus rhythm [22, 23]. Atrial fibrillation might be a manifestation of disease progression, and it may indicate the process of advanced remodeling and fibrosis, which affects not only the atria but also the ventricles. Patients with AF are often older, with more comorbidities and cardiovascular risk factors, which increase the risk of VF. The other explanation of this phenomenon is that the risk factors of AF and VF are similar, such as increased sympathetic tone, ischemia, higher left ventricular filling pressures, and decreased cardiac output. The proarrhythmic effect of antiarrhythmic drugs used in AF may be another explanation for this phenomenon. What is more, atrial fibrillation seems to be arrhythmogenic *per se*. Some recent trials showed that AF ablation reduced AF burden and improved prognosis [24].

Our analyses indicate that supraventricular tachyarrhythmias predicted ventricular arrhythmias. It is, indeed, an unexpected phenomenon, and such an association has not been previously observed. Several mechanisms could explain this observation. Based on IEGM records, it is difficult to determine precisely what kind of supraventricular arrhythmias we were dealing with. Nevertheless, atrioventricular node reentrant tachycardia (AVNRT) or atrioventricular reentry tachycardia (AVRT) are rare in HF patients. Thus, our patients' SVT episodes were usually atrial tachycardia (AT) or sinus tachycardia. Atrial tachycardia may be followed by atrial fibrillation as an expression of remodeling and fibrosis observed in the atria and ventricles. Such arrhythmias may have a pro-arrhythmogenic potential. The episodes of atrial tachycardia might also indicate HF progression. Another reasonable explanation of this phenomenon might be that these SVT episodes are sinus tachycardia recorded by the ICD (in quite frequent cases, it is impossible to define unequivocally based on the IEGM if it is sinus tachycardia or AT). This may indicate autonomic imbalance with transiently elevated sympathetic drive. Previously we observed in the TRUST trial that increased day and night rates might predict ventricular arrhythmias in patients with CRT-D [25]. Sinus tachycardia also suggests HF decompensation — another mechanism that may lead to more frequent ventricular arrhythmias.

Finally, the occurrence of ventricular arrhythmia is associated with significantly worse prognosis, with fatality rates exceeding 36%. In the DANISH trial, the SCD rate was low — less than 2% per year [5]. Nevertheless, in our study, VT/VF occurred in almost one-fourth of patients, and what is more, ventricular arrhythmias were a surrogate indicator of poor prognosis. VT/VF are life-threatening arrhythmias, but in ICD patients, in most cases, they are effectively terminated. Higher mortality in ICD patients, regardless of ischemic or non-ischemic HF, was previously observed in both primary and secondary prevention subjects if they received ICD therapy [26]. What then? There seems to be a paradox in an appropriate ICD therapy: it saves patients from fatal ventricular arrhythmias but, at the same time, shows a related risk of mortality [27]. Ventricular arrhythmias in our study were observed more often in patients with higher left ventricular dimension, atrial fibrillation/ /atrial flutter, and supraventricular tachycardia during follow-up and were associated with higher mortality. All the factors we described: VT/VF, AF/AFL, SVT (atrial tachycardia, sinus tachycardia), lower EF, and higher LVEDD, indicate the group of patients with poor prognosis. Therefore, these patients may require earlier diagnosis and more intensive treatment to improve the prognosis. ICD data provide early information on VT/VF, AF, and SVT. The feasibility of early ablation of both ventricular and supraventricular arrhythmias is still an open issue, and data for NICM patients are lacking.

Study limitations

A single-center study design is an obvious limitation of our study. A relatively small group of patients is another study limitation, but, on the other hand, the number of patients was sufficient for statistical analyses.

Changes and different device programming over time might be also a limitation of the study, but, as patients' needs may change over time, device reprogramming should be an inherent part of patient management.

CONCLUSIONS

Ventricular arrhythmia occurred in 24.4% of NICM patients during 4.5 years of observation and was associated with significantly worse prognosis than in subjects free of VT/VF. Left ventricular dimensions, atrial fibrillation/atrial flutter, and supraventricular tachycardia during follow-up were independent predictors of ventricular arrhythmia. A novel risk stratification model is needed to improve decision-making for ICD implantation in NICM patients.

Article information

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