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ORIGINAL RESEARCH

Atrial Fibrillation, Ventricular Arrhythmia, and Left Ventricular Remodeling in the ICU – First Results of the Single-Center RHYTHM-ACC Registry

Szilamér Korodi[1,2], Diana Opincariu[1,2], Annabell Benedek[1,2]

[1] University of Medicine, Pharmacy, Sciences and Technology, Tîrgu Mureș, Romania
[2] Emergency Clinical County Hospital, Tîrgu Mureș, Romania

ABSTRACT

The aim of this study was to investigate the association between left ventricular remodeling, atrial fibrillation (AF), and the severity of ventricular tachycardia (VT) in patients with ventricular rhythm disturbances admitted in a level 3 facility of acute cardiac care. **Material and Methods:** The RHYTHM-ACC registry was a single-center observational study, including 150 consecutive patients with sustained or non-sustained ventricular tachycardia (sVT and nsVT, respectively) admitted in an intensive cardiac care unit (ICCU), separated in: group 1 – 29 patients (21.01%) with dilated cardiomyopathy (DCM), and group 2 – 109 patients (78.99%) with normal ventricular performance. We investigated the difference between clinical characteristics of patients with sVT versus those with nsVT in each study group, and the association between AF and different forms of ventricular arrhythmia in 38 (25.33%) patients with AF and 112 (74.66%) patients in sinus rhythm. **Results:** There were no significant differences between the study groups with respect to type of ventricular arrhythmia: sVT (46.87% vs. 36.44%, p = 0.2), nsVT (43.75% vs. 55.93%, p = 0.2), or ventricular fibrillation (VF) (9.37% vs. 7.62%, p = 0.7). However, patients with DCM presented a significantly higher incidence of AF (43.75% vs. 20.33%, p = 0.01) and bundle branch block (37.5% vs. 11.86%, p = 0.0007). VF occurred more frequently in patients with AF compared to those in sinus rhythm (18.42% vs. 4.46%, p = 0.006). Multivariate analysis identified the co-existence of AF (OR = 4.8, p = 0.01) and the presence of a bundle branch block (BBB) (OR = 3.9, p = 0.03) as the most powerful predictors for the degeneration of VT into VF in patients admitted with sVT or nsVT in an ICCU unit. **Conclusions:** In patients with any type of VT admitted in an ICCU, the presence of ventricular remodeling is associated with a higher incidence of AF and conduction abnormalities, but not with a more severe pattern of ventricular arrhythmia. At the same time, AF and BBB seem to represent the most powerful predictors for degeneration of VT into VF, independent of the type of VT.

Keywords: sustained, non-sustained, ventricular tachycardia, atrial fibrillation, dilated cardiomyopathy

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CORRESPONDENCE

Diana Opincariu
Str. Gheorghe Marinescu nr. 50
540136 Tîrgu Mureș, Romania
Tel: +40 265 212 111
E-mail: diana.opincariu@yahoo.ro

Szilamér Korodi: Str. Gheorghe Marinescu nr. 50, 540136 Tîrgu Mureș, Romania. Tel: +40 265 212 111, E-mail: szilamerkorodi@yahoo.com
Annabell Benedek: Str. Gheorghe Marinescu nr. 50, 540136 Tîrgu Mureș, Romania. Tel: +40 265 212 111, E-mail: annabell.benedek@yahoo.com

INTRODUCTION

Cardiac remodeling represents an unfavorable pathological process associated with progressive loss of left ventricular function. Remodeling is usually caused by myocardial injury produced by an acute myocardial infarction (AMI), or an inflammatory process that leads to various cellular and molecular changes.[1,2] The clinical diagnosis of cardiac remodeling is established in the presence of ventricular dilatation associated to modifications of ventricular mass and geometry. In case of remodeling secondary to myocardial infarction, an area of scar and fibrosis can be identified at the site of infarction.[1,2] The most commonly used methods for the identification of ventricular remodeling are represented by echocardiography and cardiac magnetic resonance.[1,3]

Left ventricular dysfunction has an important impact on the prognosis of patients with AMI.[1] The mortality of patients diagnosed with left ventricular dysfunction may rise to 50% at 5 years.[4] Regardless of modern therapy, sudden death caused by malignant ventricular arrhythmias, such as sustained ventricular tachycardia (VT) and ventricular fibrillation (VF), is still significantly increased in patients with cardiac dysfunction.[5,6]

The mechanism of ventricular remodeling is not completely understood. Possible factors involved in the initiation and progression of remodeling are cardiomyocyte loss, altered energy metabolism, inflammation, oxidative stress, degradation of contractile proteins, collagen proliferation or degradation, alteration of calcium transport, and neurohormonal activation.[1] At the same time, immune reactions mediated by inflammation and oxidative stress have an important role in the development of myocardial fibrosis and cardiac remodeling, while fibrosis, as the consequence of inflammation-related tissue injury, has a crucial role in myocardial regeneration.[7–11] Several studies demonstrated that fibrotic tissue contributes to the development of reentry arrhythmia by blocking electrical conduction, thus increasing the risk of arrhythmias and sudden death.[1,12] At the same time, systemic inflammation, chronic oxidative stress, and neurohormonal activation stimulate the further development of progressive myocardial fibrosis, resulting in the deterioration of left ventricular function and heart failure (HF).[7–11]

Several studies demonstrated the association between atrial fibrillation (AF) and heart failure (HF).[7–11,13–15] In HF, neurohormonal imbalance and a dysfunctional activation of the renin-angiotensin-aldosterone system (RAAS) may represent the causal factors of the elevated afterload. Furthermore, the left atrium, being exposed to increased stretch and fibrosis, develops a structural abnormality which may intensify the alteration of atrial conduction function and contribute to the initiation and perpetuation of AF.[13,16–20]

AF and HF have recently emerged amongst the highly prevalent cardiovascular maladies affecting the general population. Often enough, they seem to be present in a conjunction associated with a multitude of diagnoses, and their simultaneous presence characterize an amplified morbidity and mortality in comparison with one singular pathology alone. The intertwinement of the two cardiac diseases can be seen in their similarities of mechanism and therapeutic attitude, thus the treatment procedures aimed towards the HF may represent a preventive factor against the development of AF.[13,14]

HF and AF are tightly linked cardiac pathologies that are simultaneous facing an increase in prevalence and incidence given their common risk factors (such as hypertension, obesity, diabetes, ischemic, non-ischemic and valvular heart disease) and similar physiopathological mechanisms.[13,14] Moreover, the favorable environment produced by alterations in the extracellular and/or intracellular compartment of the myocardial cells, adding to the neurohormonal and electrophysiological disfunctions, may result in development of the two pathologies.[15,21] The presence of both conditions accurately resemble a growth in mortality and morbidity. As treatment schemes and therapeutic strategies share a significant common ground, optimal and prompt management of one disease may reduce the chances of the other settling in.[15]

HF may cause abnormalities of the physiological function of the atrium, thus promoting the incurrence of the AF. These changes in the atrial function include irregularities of intracellular calcium levels, uplifted filling pressures and/or the dysfunction in their autonomic and neuroendocrine activity.[15,22]

The link between AF and ventricular remodeling has been extensively studied and the current evidence suggests that ventricular remodeling can lead to AF via complex mechanisms. At the same time, ventricular remodeling has been linked to occurrence of severe ventricular arrhythmia. However, there were no studies so far to investigate the association between ventricular remodeling, AF and ventricular arrhythmia.

The aim of this study was to investigate the association between left ventricular remodeling, AF and severity of VT in patients with ventricular rhythm disturbances admitted in a level 3 facility of acute cardiac care.

MATERIAL AND METHODS

The RHYTHM-ACC registry was a single-center observational study, which included 150 consecutive patients with sustained or non-sustained VT, admitted to the Clinic of Cardiology of the County Clinical Emergency Hospital of Tîrgu Mureș, Romania between January 1, 2016 and June 28, 2018. All patients were admitted to the intensive cardiac care unit (ICCU), a level 3 facility for treating acute cardiac conditions, and were transferred to the regular cardiology ward as soon as their clinical status allowed.

DATA COLLECTION

Data collection was performed during index hospitalization and included patient demographics, clinical characteristics, presence of cardiovascular risk factors, medical history, comorbidities, laboratory results (biochemistry, complete blood count, electrolyte levels), imaging data (echocardiographic assessment of left ventricular function and diameter, coronary angiography for assessment of coronary arteries, when indicated), electrocardiographic tracing (type of VT, other ventricular rhythm disturbances, supraventricular arrhythmias, atrioventricular and interventricular conduction abnormalities), and therapeutic management (interventional and pharmacological treatment).

ETHICS

All patients signed a written informed consent prior to inclusion in the study. Study procedures were conducted according to the Declaration of Helsinki, and the study protocol was approved by the ethics committee of the institution.

STUDY DESIGN

For the purpose of this study, the population of the registry was divided into 2 groups, based on the presence or absence of dilated cardiomyopathy (DCM). DCM was defined as significantly reduced left ventricular performance, with a left ventricular ejection fraction (LVEF) <40%, associated with an enlarged left ventricle, with a diameter >53 mm in women and >59 mm in men.[23] Group 1 included 29 patients (21.01%) with DCM, while group 2 included 109 patients (78.99%) with normal ventricular performance.

Ischemic heart disease was defined by the presence of at least one significant obstruction of the coronary arteries, causing a stenosis of at least 75% in a major epicardial vessel.

A further subanalysis of the registry investigated the differences between clinical characteristics of patients with sustained ventricular tachycardia (sVT) versus those with non-sustained ventricular tachycardia (nsVT) in each study group. In group 1, this subanalysis included 15 (51.72%) patients with sVT and 14 (48.27%) patients with nsVT, while in group 2 the subanalysis was performed for 43 (39.45%) patients with VT versus 66 (60.55%) patients with nsVT. Sustained VT was defined as ventricular arrhythmia with duration longer than 30 s or requiring earlier intervention for hemodynamic instability, while nsVT was defined as 3 or more consecutive beats with an RR interval of <600 ms (>100 beats/min) and lasting <30 s.[24,25] Patients who presented nsVT followed by at least one episode of sVT during hospitalization were classified as cases with sVT.

At the same time, the association between AF and different forms of ventricular arrhythmia was investigated in 38 (25.33%) patients with AF and 112 (74.66%) patients in sinus rhythm.

STATISTICAL ANALYSIS

Statistical analysis was performed with the use of GraphPad Prism 7 software (GraphPad Software, San Diego, CA, USA). Continuous variables were tested for normality by using the D'Agostino Pearson Omnibus test and were subsequently compared using Student's t test or the Mann-Whitney test when appropriate. The binary data was analyzed by using the Chi square test or its alternates when appropriate, as were expressed as integer and percentage values. The correlations between continuous variables were assessed with the Spearman or Pearson correlation coefficient when suitable. Multivariate analysis was performed in order to identify predictive factors associated with the risk of VF following an episode of VT. All the performed tests were two-tailed, and the statistical significance of the study was set at an alpha coefficient of 0.05.

RESULTS

CHARACTERISTICS OF THE REGISTRY POPULATION

Between January 2016 and June 2018, 150 consecutive patients (aged 61.83 ± 13.98 years, 66.6% males) with different forms of VT were included in the registry. Clinical characteristics of the registry population are presented in Table 1.

TABLE 1. Characteristics of the RHYTHM-ACC registry population

	Total N = 150	Group 1 – DCM N = 32 (21.33%)	Group 2 – no DCM N = 118 (78.66%)	p value
Age (years)	61.83 ± 13.98	62.66 ± 14.87	61.61 ± 13.79	0.3
Male gender, n (%)	100 (66.66%)	20 (62.5%)	80 (67.79%)	0.5
History				
Smoker, n (%)	38 (25.33%)	3 (9.37%)	35 (29.66%)	0.02
Hypertension, n (%)	98 (65.33%)	13 (40.62%)	85 (72.03%)	0.001
Diabetes, n (%)	29 (19.33%)	7 (21.87%)	22 (18.64%)	0.6
Dyslipidemia, n (%)	44 (29.33%)	7 (21.87%)	37 (31.35%)	0.2
Obesity, n (%)	6 (4%)	2 (6.25%)	4 (3.38%)	0.6
Clinical characteristics				
Creatinine (mg/dL)	1.09 ± 0.53	1.33±0.97	1.03±0.31	0.03
Ejection fraction (%)	42.39 ± 12.11	29.67±10.02	46.88±9.28	<0.0001
LVEDD (mm)	58.51 ± 9.98	69±9.39	54.91±7.31	<0.0001
NYHA class, n (%)	62 (41.33%)	28 (87.5%)	34 (28.81%)	<0.0001
CAD, n (%)	134 (89.33%)	26 (81.25%)	108 (91.52%)	0.09
AMI, n (%)	84 (56%)	11 (34.37%)	73(61.86%)	0.005
Arrhythmia type				
nSVT, n (%)	80 (53.33%)	14 (43.75%)	66 (55.93%)	0.2
SVT, n (%)	58 (38.66%)	15 (46.87%)	43 (36.44%)	0.2
VF, n (%)	12 (8%)	3 (9.37%)	9 (7.62%)	0.7
AF, n (%)	38 (25.33%)	14 (43.75%)	24 (20.33%)	0.01
Conduction disorder				
AVB, n (%)	17 (11.33%)	4 (12.5%)	13 (11.01%)	0.7
Bundle branch block, n (%)	26 (17.33%)	12 (37.5%)	14 (11.86%)	0.0007

DCM – dilated cardiomyopathy, LVEDD – left ventricular end-diastolic diameter, NYHA – New York Heart Association, CAD – coronary artery disease, AMI – acute myocardial infarction, AF – atrial fibrillation, AVB – atrioventricular block, nsVT – non-sustained ventricular tachycardia, sVT –sustained ventricular tachycardia, VF – ventricular fibrillation

The type of VT was sVT in 38.66%, nsVT in 53.33%, and VF in 8% of the cases, while 25.33% of the registry population presented co-existent AF, 17.33% bundle branch block and 11.33% atrioventricular block.

Coronary artery disease (CAD) was documented by coronary angiography in 89.33% of the registry population, 56% of the patients presenting with an acute coronary syndrome.

CLINICAL CHARACTERISTICS IN THE STUDY GROUPS

There were no significant differences between the study groups with respect to age (p = 0.3), gender (p = 0.5), and presence of diabetes (p = 0.6), dyslipidemia (p = 0.2), or obesity (p = 0.6). However, patients with DCM were less frequently smokers (9.37% vs. 29.66%, p = 0.02) and hypertensive (40.62% vs. 72.03%, p = 0.001) than patients with normal ventricular function. At the same time, they presented a more severely altered clinical status, as characterized by a significantly lower LVEF (p <0.0001), a higher incidence of advanced NYHA class (87.5% in NYHA 3 or 4 compared to 28.81%, p<0.0001), and higher levels of creatinine (1.33 ± 0.97 mg/dL vs. 1.03 ± 0.31 mg/dL, p = 0.03). CAD was present in both groups, without any significant differences between the study groups; however, the incidence of AMI was significantly lower in the DCM group (34.37% vs. 61.86%, p = 0.005).

LEFT VENTRICULAR REMODELING AND CARDIAC ARRHYTHMIA

Analysis of left ventricular remodeling identified significantly larger ventricular cavities in patients with DCM (69.0 ± 9.39 mm vs. 54.9 ± 7.31 mm, p <0.0001).

There were no significant differences between the study groups with respect to the type of ventricular arrhythmia: sVT (46.87% vs. 36.44%, p = 0.2), nsVT (43.75% vs. 55.93%, p = 0.2), or VF (9.37% vs. 7.62%, p = 0.7). However, patients with DCM presented a higher incidence of AF (43.75% vs. 20.33%, p = 0.01) and bundle branch block (37.5% vs. 11.86%, p = 0.0007).

TABLE 2. Subgroup analysis of clinical characteristics in sVT versus nsVT, according to the presence of ventricular remodeling and atrial fibrillation

	DCM N = 29 (21.01%)			No DCM N = 109 (78.99%)			AF N = 38 (25.33%)			No AF N = 112 (74.66%)		
	sVT N = 15 (51.72%)	nsVT N = 14 (48.27%)	p value	sVT N = 43 (39.45%)	nsVT N = 66 (60.55%)	p value	sVT N = 13 (37.21%)	nsVT N = 18 (47.36%)	p value	sVT N = 45 (40.17%)	nsVT N = 62 (55.35%)	p value
Age (years)	65.2 ± 12.04	58.43 ± 17.98	0.2	62.81 ± 13.39	61.02 ± 14.45	0.7	66 ± 12.13	69.28 ± 9.62	0.4	62.69 ± 13.27	58.03 ± 15.43	0.1
Male gender, n (%)	12 (80%)	7 (50%)	0.1	32 (74.41%)	42 (63.63%)	0.2	11 (84.62%)	11 (61.11%)	0.2	33 (73.33%)	38 (61.29%)	0.1
History												
Smoker, n (%)	3 (20%)	0 (0%)	0.2	16 (37.2%)	16 (24.24%)	0.1	3 (23.08%)	1 (5.56%)	0.2	16 (35.56%)	15 (24.19%)	0.2
Hypertension, n (%)	8 (53.33%)	4 (28.57%)	0.2	32 (74.41%)	49 (74.24%)	0.9	8 (61.54%)	12 (66.67%)	0.7	32 (71.11%)	41 (66.13%)	0.5
Diabetes, n (%)	4 (26.66%)	3 (21.42%)	0.9	9 (20.93%)	12 (18.18%)	0.7	3 (23.08%)	6 (33.33%)	0.6	10 (22.22%)	9 (14.52%)	0.3
Dyslipidemia, n (%)	3 (20%)	3 (21.42%)	0.9	14 (32.55%)	18 (27.27%)	0.5	2 (15.38%)	3 (16.67%)	0.9	15 (33.33%)	18 (29.03%)	0.6
Obesity, n (%)	0 (0%)	1 (7.14%)	0.4	1(2.32%)	3 (4.54%)	0.9	0 (0%)	2 (11.11%)	0.4	1 (2.22%)	2 (3.23%)	0.9
Clinical characteristics												
Creatinine (mg/dL)	1.2 ± 0.24	1.47 ± 1.42	0.2	1.05 ± 0.29	1.01 ± 0.32	0.5	1.2 ± 0.34	1.19 ± 0.61	0.2	1.06 ± 0.27	1.07 ± 0.69	0.3
Ejection fraction (%)	29.45 ± 13.0	29.3 ± 7.67	0.6	47.37 ± 9.19	47.31 ± 9.42	0.9	31.44 ± 14.92	41.89 ± 11.7	0.1	45.52 ± 10.8	43.76 ± 11.85	0.5
LVEDD (mm)	68.7 ± 9.32	68.9 ± 10.44	0.9	54.04 ± 6.55	54.64 ± 7.61	0.7	64.14 ± 12.61	58.11 ± 8.98	0.1	56.66 ± 8.57	57.65 ± 10.42	0.7
NYHA class, n (%)	12 (80%)	13 (92.85%)	0.5	9 (20.93%)	23 (34.84%)	0.1	10 (76.92%)	12 (66.67%)	0.6	11 (24.44%)	24 (38.71%)	0.1
CAD, n (%)	13 (86.66%)	10 (71.42%)	0.3	38 (88.37%)	62 (93.93%)	0.3	10 (76.92%)	17 (94.44%)	0.2	41 (91.11%)	55 (88.71%)	0.7
AMI, n (%)	8 (53.33%)	1 (7.14%)	0.01	27 (62.79%)	39 (59.09%)	0.6	6 (46.15%)	6 (33.33%)	0.4	29 (64.44%)	34 (54.84%)	0.3
Conduction disorder												
AVB, n (%)	1 (6.66%)	3 (21.42%)	0.3	2 (4.65%)	9 (13.63%)	0.1	0 (0%)	3 (16.67%)	0.2	3 (6.67%)	9 (14.52%)	0.2
Bundle branch block, n (%)	3 (20%)	7 (50%)	0.1	7 (16.27%)	4 (6.06%)	0.1	1 (7.69%)	2 (11.11%)	0.9	9 (20%)	9 (14.52%)	0.4

DCM – dilated cardiomyopathy, LVEDD – left ventricular end-diastolic diameter, NYHA – New York Heart Association, CAD – coronary artery disease, AMI – acute myocardial infarction, AF – atrial fibrillation, AVB – atrioventricular block, nsVT – non-sustained ventricular tachycardia, sVT –sustained ventricular tachycardia, VF – ventricular fibrillation

TABLE 3. Characteristics of the RHYTHM-ACC registry population based on the presence of atrial fibrillation

	Total N = 150	AF N = 38 (25.33%)	No AF N = 112 (74.66%)	p value
Age (years)	61.83 ± 13.98	67.32 ± 11.15	59.97 ± 14.39	0.002
Male gender, n (%)	100 (66.66%)	25 (65.79%)	75 (66.96%)	0.8
History				
Smoker, n (%)	38 (25.33%)	6 (15.79%)	32 (28.57%)	0.1
Hypertension, n (%)	98 (65.33%)	21 (55.26%)	77 (68.75%)	0.1
Diabetes, n (%)	29 (19.33%)	9 (23.68%)	20 (17.86%)	0.4
Dyslipidemia, n (%)	44 (29.33%)	9 (23.68%)	35 (31.25%)	0.3
Obesity, n (%)	6 (4%)	3 (7.89%)	3 (2.68%)	0.1
Clinical characteristics				
Creatinine (mg/dL)	1.09 ± 0.53	1.18 ± 0.5	1.06 ± 0.54	0.1
Ejection fraction (%)	42.39 ± 12.11	36.5 ± 12.82	44.35 ± 11.28	0.009
LVEDD (mm)	58.51 ± 9.98	61.57 ± 10.98	57.58 ± 9.54	0.1
NYHA class, n (%)	62 (41.33%)	26 (68.42%)	36 (32.14%)	<0.0001
CAD, n (%)	134 (89.33%)	34 (89.47%)	100 (89.29%)	0.9
AMI, n (%)	84 (56%)	17 (44.74%)	67 (59.82%)	0.1
Arrhythmia type				
nSVT, n (%)	80 (53.33%)	18 (43.37%)	62 (55.36%)	0.3
SVT, n (%)	58 (38.66%)	13 (34.21%)	45 (40.18%)	0.5
VF, n (%)	12 (8%)	7 (18.42%)	5 (4.46%)	0.006
Conduction disorder				
AVB, n (%)	17 (11.33%)	4 (10.53%)	13 (11.61%)	0.9
Bundle branch block, n (%)	26 (17.33%)	6 (15.79%)	20 (17.86%)	0.7

DCM – dilated cardiomyopathy, LVEDD – left ventricular end-diastolic diameter, NYHA – New York Heart Association, CAD – coronary artery disease, AMI – acute myocardial infarction, AVB – atrioventricular block, nsVT – non-sustained ventricular tachycardia, sVT –sustained ventricular tachycardia, VF – ventricular fibrillation

Interestingly, the type of ventricular arrhythmia was not associated with any of the clinical variables studied. Subgroup analysis based on the type of arrhythmia is presented in Table 2, indicating no significant differences in clinical characteristics, history, EF, conduction disorder, or ventricular remodeling between the subgroups with sVT or nsVT, in both the DCM and no-DCM groups.

ATRIAL FIBRILLATION, VENTRICULAR ARRHYTHMIA, AND VENTRICULAR REMODELING

From the total population of the registry, 25.33% (n = 38) presented AF. Clinical characteristics of the patients with AF are listed in Table 3. Patients with AF were significantly older (67.32 ± 11.1 years vs. 59.97 ± 14.39 years, p = 0.002), presented more frequently NYHA 3 or 4 class (68.42% vs. 32.14%, p <0.0001), and had a significantly lower EF (36.5 ± 12.82% vs. 44.35 ± 11.28%, p = 0.009) than patients without AF (Figure 1). However, the extent of left ventricular remodeling was not significantly different between patients with or without AF, as shown by a similar degree of left ventricular enlargement (61.57 ± 10.98 mm vs. 57.58 ± 9.54 mm for LVEDD, p = 0.1).

In the AF-subgroup analysis of the registry population, the type of VT, sustained or non-sustained, was not associated with any of the clinical variables studied (Table 2). However, VF occurred more frequently in patients with AF than in those in sinus rhythm (18.42% vs. 4.46%, p = 0.006), and VF was the only type of ventricular arrhythmia associated with AF (Figure 2).

PREDICTORS OF VF IN THE POPULATION OF THE RHYTHM-ACC REGISTRY

Multivariate analysis of predictors for the occurrence of VF in the registry population identified the co-existence of AF (OR = 4.8, p = 0.01) and the presence of a bundle branch block (OR = 3.9, p = 0.03) as the most powerful predictors for the degeneration of VT into AF in patients admitted to an ICCU with sVT or nsVT, with a prediction power superior to the presence of CAD (OR = 1.3, p = 1), AMI (OR = 2.5, p = 0.2), DCM (OR = 1.2, p = 0.7), or sVT (OR = 1.3, p = 0.7) (Table 4).

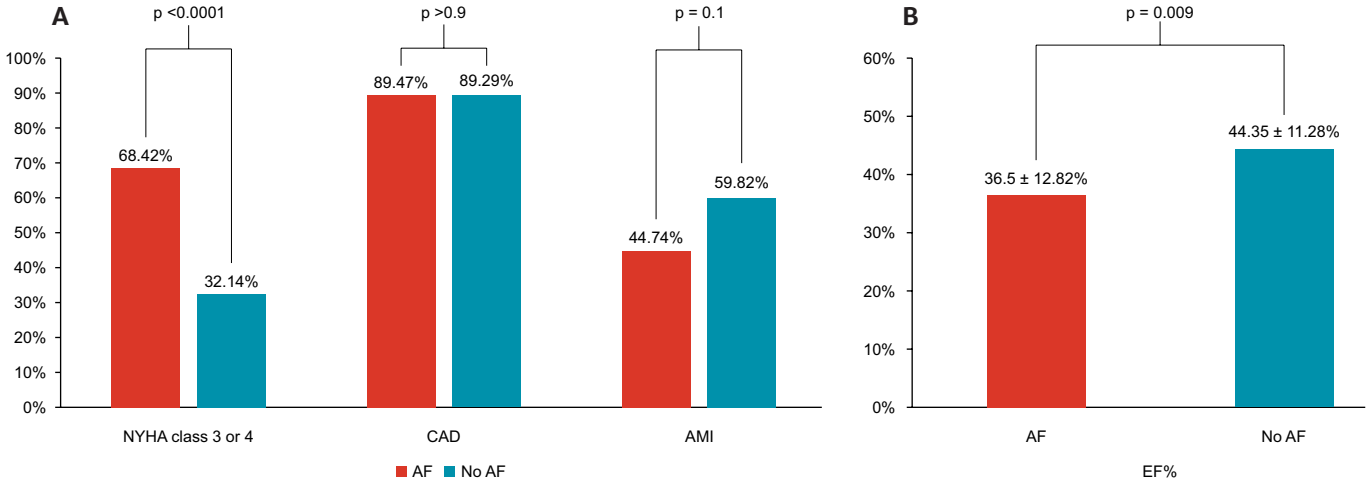

FIGURE 1. Clinical characteristics of patients with atrial fibrillation and ventricular tachycardia. **A** – incidence of advanced heart failure, CAD, and AMI in patients with AF versus no AF; **B** – ejection fraction in patients with AF versus no AF. NYHA – New York Heart Association, CAD – coronary artery disease, AMI – acute myocardial infarction, AF – atrial fibrillation, EF – ejection fraction

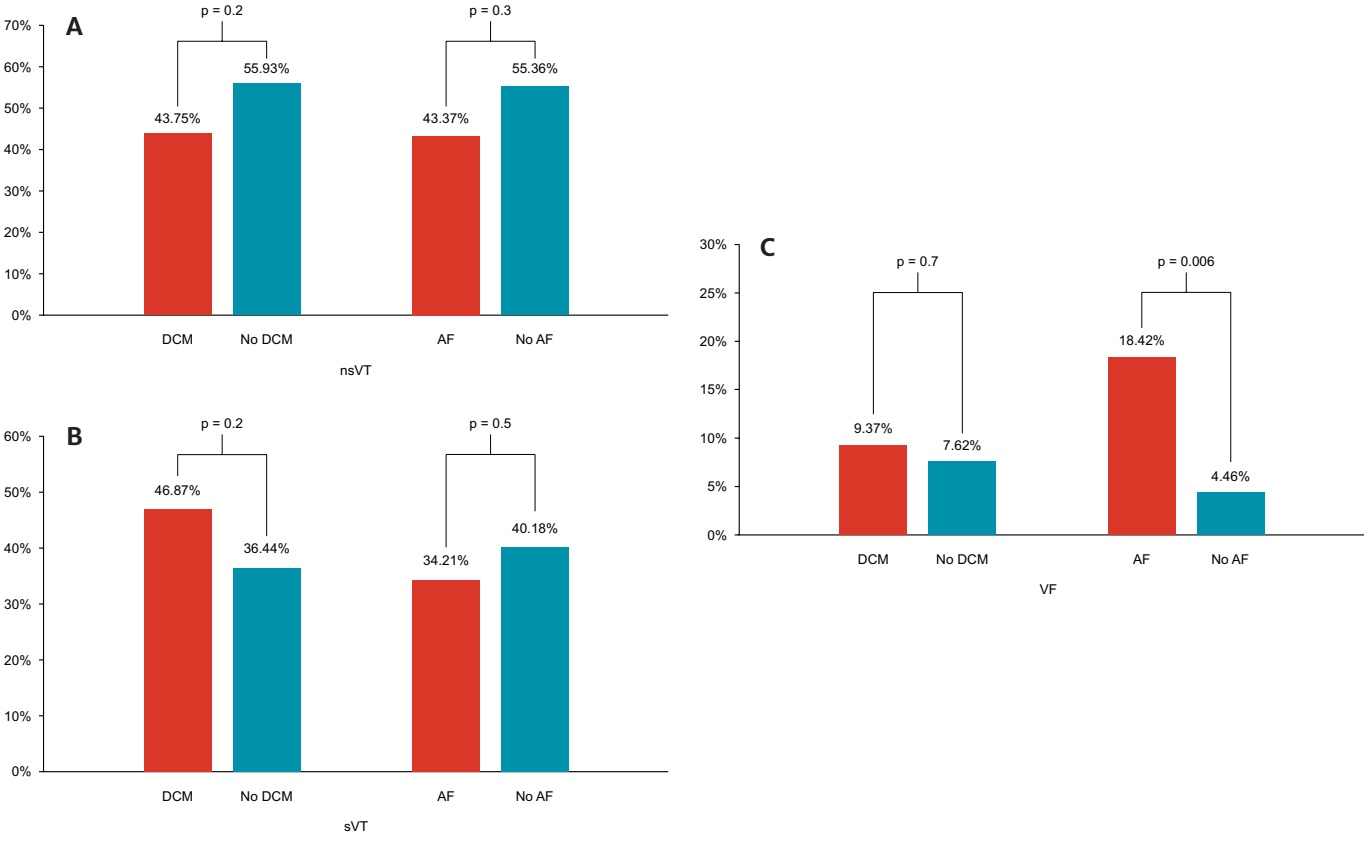

FIGURE 2. Incidence of different types of VT in the population of the RHYTHM-ACC Registry. **A** – Incidence of nsVT in the study population – no significant association between nsVT and DCM or AF; **B** – Incidence of sVT in the study population – no significant association between sVT and DCM or AF; **C** – Incidence of VF in the study population – significant association between AF and VF, indicating that the concomitant presence of AF and VT is associated with a significantly higher risk of arrhythmia degeneration into VF. DCM – dilated cardiomyopathy, AF – atrial fibrillation, nsVT – non-sustained ventricular tachycardia, sVT – sustained ventricular tachycardia, VF – ventricular fibrillation

TABLE 4. Multivariate analysis of predictors for VF in patients with VT

Characteristic	OR (95% CI)	p value
Coronary artery disease	1.34 (0.1–11.1)	1
Acute myocardial infarction	2.5 (0.6–9.7)	0.2
Atrial fibrillation	4.8 (1.4–16.2)	0.01
Atrioventricular block	1.6 (0.3–8.2)	0.6
Bundle branch block	3.9 (1.1–13.7)	0.03
Non-sustained ventricular tachycardia	0.7 (0.2–2.3)	0.7
Sustained ventricular tachycardia	1.37 (0.4–4.4)	0.7
Dilated cardiomyopathy	1.25 (0.3–4.9)	0.7
NYHA class 3 or 4	1.22 (0.3–8.2)	0.6

DISCUSSIONS

Ventricular rhythm disturbances are the main cause of sudden cardiac deaths, being more frequently encountered in patients with structural heart diseases and impaired left ventricular function. Significant CAD and myocardial infarction with subsequent scarring may also lead to sVT, triggered by reentry as the main electrophysiological mechanism.[26] On the other hand, nsVT can occur in structurally normal hearts or in severe heart diseases as well, being associated with a worse prognosis.[27]

Ventricular arrhythmias, ranging from premature ventricular beats to nsVT, sVT, or VF, are more likely to cause sudden cardiac death if occurring in the context of myocardial ischemia, especially in the elderly population.[28,29] In our study cohort, the vast majority of subjects (89.33%) presented significant CAD at invasive coronary angiography, and a significant proportion were admitted with different forms of acute coronary syndromes.

LEFT VENTRICULAR REMODELING, DILATED CARDIOMYOPATHY, AND VENTRICULAR ARRHYTHMIA

The main study group analysis revealed no differences between patients with or without DCM in relation to demographics or cardiovascular risk factors. As expected, DCM patients presented significantly lower LVEF (%), higher NYHA class, and higher rates of renal function impairment, but compared to non-DCM patients they were less likely to present AMI, despite the lack of any significant difference with respect to the presence of CAD. This could indicate an alternative, non-ischemic etiology of the DCM.[30,31] However, as the etiology was not investigated in the present study, this observation remains speculative.

There was no difference between the DCM and non-DCM groups with respect to the type of ventricular arrhythmias (p = 0.7); nevertheless, DCM patients presented higher rates of AF (p = 0.01) and bundle branch block (p = 0.0007), both of which may have occurred either as a cause or a consequence of DCM. A rare cause of bundle branch block associated with VT is the bundle branch reentrant tachycardia, typically occurring in patients with structural heart disease, but most of the reported cases included subjects with ischemic and non-ischemic DCM.[32,33]

Patients with AMI are at high risk of developing sustained VT in the peri-infarction period, due to abnormal automaticity, re-entrant circuits, delayed depolarization, and heterogeneous repolarization.[34] LVEF is currently considered the most powerful predictor for sudden cardiac death following an AMI, being also one of the main criteria for decision towards the implantation of an intracardiac defibrillator.[35,36]

Interestingly, the type of ventricular arrhythmia was not associated with any clinical characteristic of the study population in our registry, but patients with DCM and AMI were more likely to present sVT (p = 0.01), an association that was not present in the case of subjects with non-DCM and AMI (p = 0.699).

ATRIAL FIBRILLATION AND THE RISK OF VENTRICULAR ARRHYTHMIA

A subanalysis of the RHYTHM-ACC registry aimed to investigate the effect of AF on the occurrence of sVT and nsVT, respectively. As expected, patients who presented supraventricular arrhythmia were older, with a more severely altered clinical status and lower EF. Interestingly, the degree of left ventricular remodeling did not differ among patients with and without AF, which could raise several questions on the cause of AF in this registry cohort, as well as its longevity. AF with a rapid ventricular response of over 100 beats per minute has been incriminated as one of the causes of tachycardia-induced cardiomyopathy. This condition is characterized by reversible cardiac remodeling due to increased heart rate and subsequent elevated filling pressures, which leads to decreased contractility, reduction of cardiac output, and neurohormonal activation.[37,38] The subsequent lowering of left ventricular performance, associated with increased neurohormonal activation could represent a cause of ventricular arrhythmias, triggering a vicious cycle in which the "AF begets AF" phenomenon could be transposed into the ventricular region: "AF begets VT/VF".[39–41]

Additionally, AF subjects were significantly more likely to develop VF compared to those in sinus rhythm.

Moreover, in the multivariate analysis, the most powerful predictors for developing VF in patients admitted with sVT or nsVT were the presence of AF or bundle branch block.

A study conducted by Link *et al*. (2017) found that in patients with hypertrophic cardiomyopathy, the occurrence of ventricular tachyarrhythmias was preceded by rapid supraventricular rhythms, including rapid ventricular response AF. The possible explanation for this observation could rely on the increased sympathetic stimulation that triggers the supraventricular arrhythmia, leading to VT or VF.[42] Several case reports have also indicated that in patients with intracardiac defibrillators implanted for ventricular tachyarrhythmias, paroxysmal episodes of AF had triggered several episodes of sVT or nsVT, with consequent delivery of intracardiac shock therapy.[43-45] All these observations are in line with the results of our study, which suggests that in patients with sVT or nsVT, the co-existence of AF or bundle branch block increases the risk of VT degeneration into VF. According to the authors' knowledge, this is the first study reporting a direct link between left ventricular remodeling, AF, conduction disturbances, and the occurrence of severe ventricular arrhythmia.

STUDY LIMITATIONS

In this study, all data were collected only during hospitalization for the index event, and there are no follow-up data processed so far to assess the risk of VT recurrence or the incidence of malignant ventricular arrhythmia on short or long term. Collection of follow-up data is currently ongoing, and it will contribute to further development of the RHYTHM-ACC Registry.

CONCLUSIONS

The RHYTHM-ACC registry demonstrated that in patients admitted to an ICCU and presenting any type of VT, the presence of ventricular remodeling is associated with a higher incidence of AF and conduction abnormalities, but not with a more severe pattern of ventricular arrhythmia. At the same time, AF and bundle branch block seem to represent the most powerful predictors for the degeneration of VT into VF, independent of the type of VT.

CONFLICT OF INTEREST

Nothing to disclose.

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