Atrial fibrillation and elevated heart rate: Independent prognostic factors of right ventricular dysfunction in patients with heart failure with reduced ejection fraction

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INTRODUCTION

Heart failure with reduced ejection fraction (HFrEF) is diagnosed when left ventricular ejection fraction (LVEF) is less than 40% in patients with adequate symptoms and signs. As the disease progresses, atrial fibrillation (AF) occurs in up to 50% of patients [1, 2]. We have shown before that in patients with AF, right ventricular function (RV) is worse [3]. The current study aimed to search for independent prognostic factors of depressed RV function in patients with HFrEF and AF.

METHODS

This was an observational, case-control, two-center study. Patients were recruited in the years 2013–2016.

Patients with HFrEF of ischemic etiology, on optimal current heart failure medical therapy, the New York Heart Association (NYHA) class II–III, LVEF ≤40%, with sinus rhythm (SR) or permanent AF for at least one year, underwent echocardiography to assess RV. All the patients had two- and three-dimensional echocardiography (2DE and 3DE; sonograph Phillips iE33 xMATRIX; Phillips Medical Systems, Netherlands, transducer iE33 X5-1). Right ventricular ejection fraction (RVEF) was assessed on three-dimensional echocardiography (4 D RV-Function 2.0 TomTec Imaging Systems GmbH, Munich, Germany).

Independent prognostic factors of depressed RVEF <45% were searched. The following variables were analyzed: age, sex, body mass index, NYHA class, history of percutaneous intervention (PCI) and coronary by-pass grafting (CABG), diabetes, arterial hypertension, systolic and diastolic blood pressure, chronic kidney disease, thyroid disease, history of stroke or transient ischemic attack, left ventricular end-diastolic diameter, left ventricular ejection fraction, presence of significant mitral or aortic regurgitation, heart rate (HR), right ventricular pacing, and cardiac resynchronization therapy. The study was supported by the State Committee for Scientific Research grant (3/5/VII/2013). The design and protocol of the study were approved by the institutional Ethics Committee at the National Institute of Cardiology, Warsaw (IK-NP-0021-28/1365/13, IK-NP-0021-7/1365/14).

Statistical analysis

The results are presented as mean and standard deviation (SD) (continuous variables with normal distributions — the Shapiro–Wilk test) or counts and frequencies. Baseline characteristics are compared using the t-test, the χ^2 test, or the Fisher exact test. To identify independent factors of depressed right ventricular function (defined as RVEF <45%), multivariable logistic regression was performed. The stepwise variable selection procedure was used. Odds ratios with 95% confidence intervals (CI) were calculated. The statistical software package (SAS 9.4, Cary, NC, US) was used for the analysis.

RESULTS AND DISCUSSION

Clinical and echocardiographic characteristics of the study group (n = 126 patients) have been published before [3]. In the AF group (94 patients), the mean HR was higher than in the SR group (32 patients), 76.7 (13)

Table 1. Patients' characteristics stratified by right ventricular dysfunction. Results of univariable and multivariable logistic regression to identify independent prognostic factors of right ventricular ejection fraction <45%

	Univariable analysis				Multivariable analysis	
	RVEF <45% (n = 85)	RVEF ≥45% (n = 31)	OR (95% CI)[a]	*P*[b]	OR (95% CI)[a]	*P*[b]
Age, years, mean (SD)	72.9 (8.4)	71.6 (9.4)	1.019 (0.971–1.068)	0.44	—	
Male sex, n (%)	76 (89.4)	27 (87.1)	1.251 (0.356–4.397)	0.73	—	
BMI, kg/m^2, mean (SD)	27.8 (4.5)	27.2 (4.9)	1.031 (0.940–1.130)	0.52	—	
HF NYHA class III, n (%)	30 (35.3)	5 (16.1)	2.836 (0.987–8.149)	0.053	—	
History of PCI, n (%)	51 (60.0)	25 (80.6)	0.360 (0.134–0.970)	0.043	—	
History of CABG, n (%)	21 (24.7)	4 (12.9)	2.215 (0.694–7.065)	0.18	5.53 (1.341–2.80)	0.018
Diabetes, n (%)	25 (29.4)	11 (35.5)	0.758 (0.317–1.810)	0.53	—	
Arterial hypertension, n (%)	61 (71.8)	19 (61.3)	1.605 (0.677–3.806)	0.28	—	
Chronic kidney disease, n (%)	27 (31.8)	6 (19.3)	1.940 (0.713–5.279)	0.19	—	
Thyroid disease, n (%)	19 (22.3)	3 (9.7)	2.687 (0.736–0.913)	0.13	—	
History of stroke, n (%)	18 (21.2)	1 (3.2)	7.123 (0.958–52.96)	0.055	—	
LVEDD, cm, mean (SD)	6.1 (1.0)	5.7 (0.9)	1.610 (1.049–2.472)	0.029	—	
LVEF, %, mean (SD)	28.2 (8.5)	30.6 (7.3)	0.963 (0.914–1.015)	0.16	—	
MR (≥III), n (%)	25 (30.1)	6 (19.3)	1.796 (0.656–4.916)	0.25	—	
AF, n (%)	74 (87.1)	12 (38.7)	10.65 (4.07–7.84)	0.01	9.14 (3.20–6.12)	<0.001
HR, bpm, mean (SD)	77.2 (13.0)	69.4 (10.2)	1.058 (1.018–1.101)	0.005	1.07 (1.02–1.13)	0.006

The results are presented as mean values and standard deviations or counts and proportions or odds ratios with a 95% confidence interval. [a]Risk of right ventricular dysfunction for increasing the feature by one unit or for the category "yes" vs. "no". [b]*P*-value for the likelihood ratio test

Abbreviations: AF, atrial fibrillation; BMI, body mass index; CABG, coronary artery bypass grafting; HF, heart failure; HR, heart rate; LVEDD, left ventricular end-diastolic dimension; LVEF, left ventricular ejection fraction; MR, mitral regurgitation; NYHA, New York Heart Association class; PCI, percutaneous coronary intervention; RVEF, right ventricular ejection fraction

bpm vs. 70.2 (9.5) bpm, respectively; *P* = 0.003. In the AF group, more patients had significant mitral and tricuspid regurgitation, and mean right ventricular systolic pressure was higher (Supplementary material, *Table S1*). A reliable analysis of 3DE data was possible in 116 patients (30 in the SR group, 86 in the AF group). In the AF group, RVEF was worse than in SR group, 37.2% (7.3%) vs. 48.2% (7.5%), respectively; *P* <0.0001. Among other analyzed parameters of RV function, longitudinal strain of RV free wall acquired while analyzing 3DE data sets and s' in 2DE were worse in the AF group (Supplementary material, *Table S1*). Only a few correlations between 2DE and 3DE were found (Supplementary material, *Table S2*). RVEF <45% was found in 74 patients with AF (86.1%) and 11 patients with SR (36.7%). Multivariable analysis of the whole study group (both AF and SR patients) showed that AF, HR, and history of CABG were independent predictors of RVEF <45% (Table 1 and Supplementary material, *Figure S1*). Odds ratios (OR) were for AF — 9.14 (3.20–26.12); *P* <0.001; for HR (by one beat per minute) — 1.07 (1.02–1.13); *P* = 0.006; for CABG — 5.53 (1.34–22.80); *P* = 0.018. The area under the curve (AUC; 95% CI) for the model was 0.83 (0.74–0.92). An increase in HR by five beats per minute was associated with an OR of 1.42 (1.11–1.78); *P* = 0.006 of RVEF <45% in the whole study group (both AF and SR). Multivariable analysis made only in the patients with AF showed that only HR was an independent factor of RVEF <45%: OR (95% CI), 1.06 (1.003–1.12); *P* = 0.037; AUC (95% CI), 0.69 (0.53–0.84). An increase in HR by five beats per minute was associated with an OR of 1.35 (1.10–1.78); *P* = 0.037 in the AF group. In the SR group, the only prognostic factor of RVEF <45% was CABG, 7.08 (1.07–46.7); *P* = 0.042; AUC, 0.675 (0.505–0.844). In this group HR was not found to be a prognostic factor of RVEF <45% in univariable analysis: OR (95% CI), 1.02 (0.94–1.10); *P* = 0.62. However, the analysis could only be made in 30 patients who had a reliable 3DE, and only 11 of them presented RVEF <45%.

It is debatable what was a direct cause of right ventricular dysfunction in the AF group. In both AF and SR groups, direct damage due to ischemia or RV dysfunction as an effect of interventricular interdependence was possible. However, impaired RV function may be a marker of a more advanced stage of HFrEF, similarly to AF. Patients with HFrEF and AF may be more prone to volume and, subsequently, pressure overload. When its compensation capacity expires, the RV dilates, and its myocardial contractility deteriorates. An increase in HR maintains cardiac output but also increases myocardial strain and oxygen demand, which leads to decompensated RV failure [4]. RV dysfunction may also result from a primary reduction of myocardial contractility due to arrhythmia, which leads to impaired RV filling and increased right atrial pressures and tricuspid regurgitation [5]. RV failure has been repeatedly shown to compromise the prognosis in heart failure. In a recent study, it was confirmed to be an independent prognostic factor of all-cause mortality and rehospitalization for heart failure [6]. It underlines the need for the search for therapies focused on preserving RV function in heart failure. The patients in this study were recruited in the years 2013–2016. Since that time new therapeutic agents have been introduced to the standard treatment of heart failure. A few studies showing an RV function improvement

and clinical short-term outcomes in patients treated with sacubitril/valsartan have been published [7, 8]. Other agents are at the stage of clinical trials. We are aware of other study limitations — the small number of patients in the two-center study and the observational design of the study with no prospective assessment. Further research is needed to establish the clinical value of the presented observations.

Supplementary material

Supplementary material is available at https://journals.viamedica.pl/kardiologia_polska.

Article information

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