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Original Research Article

Heart failure with reduced ejection fraction: differences between atrial fibrillation and sinus rhythm

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ABSTRACT

Background: Atrial fibrillation (AF) is a common comorbidity in heart failure with reduced ejection fraction (HFrEF), with prevalence ranging from 10% to 60%. While AF is generally associated with increased mortality in HF, its impact on HFrEF outcomes remains uncertain. This study evaluates clinical, laboratory and echocardiographic differences between HFrEF patients with and without AF.
Methods: This study included 91 patients (Left ventricular ejection fraction<50%) admitted to Grodno State Cardiological Centre from January to November 2024. Patients were divided into two groups: 57 (63%) with AF (paroxysmal or persistent) and 34 (37%) with sinus rhythm (SR). Clinical, laboratory and echocardiographic data were analysed using STATISTICA 12.0.
Results: AF patients had higher BMI (p=0.005) and obesity prevalence (62% vs 26%, p=0.001). Hypertension and diabetes rates were similar, but SR patients had more stable angina (53% vs 34%, p=0.03) and prior myocardial infarction (44% vs 26%, p=0.048). AF patients showed worse renal function (higher urea, creatinine and lower eGFR). Echocardiography revealed larger left (p=0.03) and right atria (p=0.017) in AF, while SR patients had a higher contractility index (p=0.032).
Conclusions: HFrEF patients with SR more often had ischemic cardiomyopathy, while those with AF had a dilated or mixed origin, as reflected in atrial size and contractility differences.

Keywords: Atrial fibrillation, Heart failure, Reduced ejection fraction, Sinus rhythm

INTRODUCTION

Heart failure (HF), which is characterized by either systolic or diastolic dysfunction, is a complex clinical disease that is becoming more and more common worldwide.[1] This complex clinical syndrome, which is characterized by a range of symptoms (dyspnea, orthopnoea and lower limb swelling) and indicators (pulmonary congestion and elevated jugular venous pressure), is caused by a structural and functional impairment of ventricular filling or blood ejection.[2] International guidelines classify HF into three subcategories heart failure with reduced left ventricular ejection fraction (HFrEF, ejection fraction (EF)<40%), heart failure with preserved left ventricular ejection fraction (HFpEF, EF>50%) and HF with mildly reduced left ventricular ejection fraction (HFmrEF, EF 40%–49%.[3]

Research has indicated that coronary artery disease (CAD) and myocardial infarction are more likely to cause HFrEF, while atrial fibrillation (AF), diabetes and obesity are risk factors for HFpEF.[4] The most prevalent prolonged arrhythmia in patients with and without heart failure (HF) is atrial fibrillation (AF), which affects up to 50% of heart failure patients and 1% to 2% of the general population.[5] The incidence of AF in HF has been rising and its existence

significantly affects the course and result of treatment.[6] Rapid and random electrical activity in the atria, which is manifested by an irregular heartbeat and absent p-waves on an electrocardiogram (ECG), is the hallmark of AF.[7] HF and AF are becoming more common, which raises mortality rates and medical expenses.

They have a close association since they share risk factors and underlying causes.[3] The worldwide THESUS-HF registry revealed some intriguing findings, including a noticeably greater occurrence of AF in HFmrEF (28.5%) as opposed to HFpEF (21.3%) and HFrEF (14.5%).[7] HFrEF is being increasingly associated with a higher risk of ischemic stroke, even in the absence of AF.[1]

Therefore, aim of our study was to evaluate impact of AF on the clinical, laboratory and echocardiographic parameters in patients with HFrEF.

METHODS

In this study, we present data collected from 91 patients who were admitted to the Grodno Regional Clinical Cardiological Centre (Grodno, Belarus) for treatment from January to November 2024.

Inclusion criteria

Inclusion criteria were age≥18 years, symptomatic HF in New York Heart Association (NYHA) functional class II-IV, LVEF<50% with evidence of structural heart disease and elevated N-terminal pro–B-type natriuretic peptide (NT-proBNP) ≥450 pg/ml.

We divided these patients into two groups. Group 1 included 57 (63%) patients with HF and paroxysmal or persistent form of AF while Group 2 included 34 (37%) patients with HF and sinus rhythm (Table 2).

Exclusion criteria

Exclusion criteria All patients underwent clinical, laboratory and instrumental studies, including transthoracic echocardiography.

Echocardiography was performed on Phillips iE33 device with a multi-frequency sensor (frequency 2.5-5.0 MHz). The examination was performed with the patient lying on his left side with his back to the researcher or on his back. The study protocol included the following indicators: left atrium (LA) and right atrium (RA) diameter in 2-chamber and 4-chamber mode, end-systolic diameter and end-diastolic diameter (mm) of the left ventricle (LV), LVEF, assessment of the state of the valvular apparatus of the heart, degree of regurgitation on the valves.

Statistical analysis

Statistical analysis was performed using the STATISTICA 12.0 software package with a preliminary check for normal distribution using a distribution histogram. Quantitative data, the distribution of which was not normal, were given as a median, 25% and 75% quartiles. Since most of the quantitative characteristics did not obey the normal distribution law, non-parametric methods were used for comparison.

The Mann-Whitney test was used to assess differences in quantitative traits between two independent groups. At a significance level of p less than 0.05, it was believed that the studied indicator in the compared groups had statistically significant differences. To compare the diagnostic value of indicators that showed statistically significant differences between groups, ROC curves of sensitivity and specificity were constructed.

The study was performed in accordance with good clinical practice standards and the principles of the declaration of Helsinki. Written informed consent was obtained from all participants prior to inclusion in the study.

RESULTS

Patients with AF and sinus rhythm were comparable in age (62 (56; 69) vs 60 (55; 67) years, p>0.05) and gender (male patients 83% vs 91%, p>0.05). Patients with HFrEF and AF had significantly higher body mass index (31 (27, 35) vs 27 (25, 30) kg/m2, p=0.005) and more often had obesity (62% vs 26%, p=0.001) than patients with HFrEF and sinus rhythm. Patients of both had no difference in prevalence of hypertension (88% vs 79%, p>0.05) and diabetes mellitus (29% vs 23%, p>0.05). It is interesting to say, that patients with HFrEF and sinus rhythm more often had stable angina (53% vs 34%, p=0.03) and more often suffered from myocardial infarction (44% vs 26%, p=0.048) than patients with HFrEF and AF. However, patients of both groups had no statistically significant differences in NYHA HF Class.

Laboratory parameters of patients didn't demonstrate any significant differences, except for renal function tests. Patients with HFrEF and AF had significantly higher levels of urea (p=0.007), creatinine (p=0,018) and slightly lower eGFR (p=0.06). The rest of the parameters of clinical blood count and biochemical blood test as well as D-Dimers and NT-proBNP levels were comparable (p>0.05).

According to the results of transthoracic echocardiography, patients with HFrEF and AF had significantly higher LA and RA diameters in both 2-chamber and 4-chamber positions (p<0.05) than patients with sinus rhythm. However, patients didn't have differences in LV linear and volumetric parameters as well as LVEF (p>0.05) with the only exclusion being end-diastolic diameter in B-Mode, which was higher in patients with sinus rhythm (p=0.04). Contractility index was also higher in patients with sinus rhythm (1.72 (1.38; 2.13) vs 1.51 (1.19; 1.81), p=0.032), correlating with higher rate of MI in this group of patients. Patients with HFrEF and AF also were characterized by higher grade of both mitral and tricuspid regurgitation (p<0.05).

Table 1: Subcategories of heart failure according to ejection fraction.

Subcategories	Ejection fraction
HFrEF	<40%
HFpEF	>50%
HFmrEF	40%-50%

Table 2: Demographic data of the study.

Characteristics	N
Participants	91
Group 1 (AF)	57
Group 2 (SR)	34

Table 3: Clinical characteristics of patients.

Parameters	AF (n=57)	SR (n=34)	p
Male gender, N (%)	48 (82.75)	31 (91.1)	0.581
Age, years, (Me (25%, 75%))	62 (56, 69)	60 (55, 67)	0.728
Body mass index, kg/m2, (Me (25%, 75%))	31 (27, 35)	27 (25, 30)	0.005
Obesity, N (%)	36 (62.1)	9 (26.4)	<0.001
Class 1, N (%)	17 (29.3)	7 (20.58)	0.334
Class 2, N (%)	13 (22.41)	2 (5.88)	0.036
Class 3, N (%)	6 (10.34)	0 (0)	0.051
Overweight, N (%)	11 (18.9)	14 (41.17)	0.020
Hypertension, N (%)	51 (87.9)	27 (79.4)	0.185
Stage 1, N (%)	4 (6.8)	4 (11.76)	0.440
Stage 2, N (%)	44 (75.9)	22 (64.7)	0.197
Stage 3, N (%)	3 (5.17)	1 (2.94)	0.602
Stable angina, N (%)	20 (34.4)	18 (52.9)	0.030
Myocardial infarction history, N (%)	15 (25.8)	15 (44.1)	0.048
Diabetes mellitus, N (%)	17 (29.3)	8 (23.5)	0.516
Heart failure NYHA Class	-	-	-
Class 1, N (%)	0 (0)	0 (0)	1.000
Class 2, N (%)	6 (10.3)	8 (23.52)	0.097
Class 3, N (%)	42 (72.4)	20 (58.82)	0.081
Class 4, N (%)	8 (13.79)	5 (14.7)	0.930

Table 4: Laboratory parameters of patients (Me (25%, 75%)).

Parameters	AF (n=57)	SR (n=34)	p
RBC, 10^{12}/l	4.82 (4.39, 5.41)	4.62 (4.3,5.1)	0.327
Hemoglobin, g/l	140.4 (131, 160)	142.5 (132, 156)	0.972
WBC, 10^9/l	7.6 (6.0, 9.0)	7.7 (5.5, 8.4)	0.518
ESR, mm/h	13.5 (4, 13.5)	10.8 (4, 10)	0.562
Urea, mmol/l	9.85 (5.9, 8.9)	6.48 (4.1, 7.3)	0.007
Creatinine, µmol/l	103.2 (87, 118.6)	116.4 (73, 106)	0.018
eGFR, ml/min/1.73 m^2	69.2 (51.8, 84.3)	78.9 (64, 95)	0.060
Cholesterol, mmol/l	6.81 (2.9, 5.3)	3.99 (2.98, 4.58)	0.940
Glucose, mmol/l	7.13 (5.2, 8.4)	7.89 (5.3, 7.9)	0.687
AST, IU/ml	24.0 (18, 25)	34.8 (15.7, 32.5)	0.833
ALT, IU/ml	29.4 (18, 34.3)	32.8 (15.5, 31.2)	0.360
Sodium, mEq/l	141.5 (139, 144)	178.6 (137, 142)	0.289
Potassium, mEq/l	4.7 (4.3, 5.1)	4.6 (4.2, 4.9)	0.249
NT-proBNP, pg/ml	5036.8 (1317, 6039)	4507 (1140, 4299)	0.638
D-Dimers, ng/ml	1370.3 (223, 1227)	2122.9 (389, 3342)	0.356

Abbreviations: RBC–red blood cells, WBC–white blood cells, ESR–erythrocyte sedimentation rate, eGFR–estimated glomerular filtration rate, AST-aspartate aminotransferase, ALT-alanine aminotransferase, NT-proBNP–N-terminal pro b-type natriuretic peptide.

Table 5: Echocardiographic parameters of patients (Me (25%,75%)).

Parameter	AF (n=57)	SR (n=34)	P value
LA diameter (2 chamber), mm	47.22 (44, 51)	45.85 (41, 48)	0.056
LA diameter (medial to lateral), mm	47.28 (44, 50)	45.55 (42, 47)	0.030
LA diameter (front to back), mm	63.89 (61, 68)	60.91 (54, 64)	0.004
RA diameter (medial to lateral), mm	44.36 (42, 46)	42.91 (39, 46)	0.017
RA diameter (front to back), mm	60.82 (57, 63)	55.44 (48, 60)	<0.001
LV ESD, mm	48.26 (44, 52)	49.6 (41, 57)	0.548
LV EDD, mm	61.1 (57, 64)	62.51 (56, 67)	0.249
M-mode			
LV ESV, ml	109.32 (84, 125)	127.22 (76, 172)	0.360
LV EDV, ml	189.6 (162, 210)	214.93 (163, 241)	0.126
LVEF, %	40.78 (36, 47)	38.1 (29, 49)	0.571
B-mode			
LV ESV, ml	111.85 (85, 129)	132.36 (96, 156)	0.084
LV EDV, ml	183.64 (150, 206)	205.27 (173, 218)	0.040
LVEF, %	39.80 (35, 46)	38.09 (33, 46)	0.423
Septal thickness (systolic), mm	15.24 (13, 16)	15.45 (14, 17)	0.640
Septal thickness (diastolic), mm	12.57 (11, 14)	12.78 (11, 14)	0.745
Posterior wall thickness (systolic), mm	15.29 (14, 16)	14.5 (13, 16)	0.213
Posterior wall thickness (diastolic), mm	11.63 (11, 12)	11.15 (10, 12)	0.293
Right ventricle diameter, mm	30.07 (27, 32)	29.87 (26, 32)	0.181
TAPSE	12.9 (8.5, 16)	15.18 (11, 16.5)	0.438
Contractility index	1.51 (1.19, 1.81)	1.72 (1.38, 2.13)	0.032
Pericardial effusion, N (%)	0 (0)	2 (5.88)	0.645
Pleural effusion, N (%)	9 (15.5)	3 (8.8)	0.581
MR grade 1, N (%)	5 (8.62)	7 (20.58)	0.108
MR grade 2, N (%)	42 (72.4)	18 (52.9)	0.044
MR grade 3, N (%)	10 (17.24)	8 (23.52)	0.489
TR grade 1, N (%)	6 (10.34)	11 (32.35)	0.010
TR grade 2, N (%)	42 (72.41)	13 (38.23)	<0.001
TR grade 3, N (%)	7 (12.06)	8 (23.5)	0.162
TR grade 4, N (%)	0 (0)	0 (0)	1.000

Abbreviations: LA–left atrium, RA–right atrium, LV–left ventricle, ESD–end-systolic diameter, EDD–end-diastolic diameter, ESV–end-systolic volume, EDV–end-diastolic volume, LVEF–left ventricular ejection fraction, MR–mitral regurgitation, TR–tricuspid regurgitation.

DISCUSSION

In this study, it was observed that patients with HFrEF and AF exhibited a significantly higher body mass index and a greater prevalence of obesity compared to those with HFrEF and sinus rhythm. Substantial evidence highlights the connection between obesity and AF, which is influenced by various intertwined mechanisms. These include diastolic dysfunction, inflammation and infiltration within epicardial adipose tissue, as well as broader systemic inflammation.[8,9]

The prevalence of hypertension and diabetes mellitus did not differ significantly between the two groups. However, these conditions are taken into account, as they, alongside obesity, represent significant risk factors for the development of HF.[10–12]

Patients with HFrEF and sinus rhythm were observed to experience stable angina and myocardial infarction more often compared to those with HFrEF and AF. Interestingly, despite anticoagulant therapy, AF patients displayed a notable residual risk of myocardial infarction.[13–15] However, findings from our studies challenge this notion, suggesting that the association between heart failure and AF could potentially lower the risk of myocardial infarction.

Laboratory parameters did not reveal significant differences between the groups, except in renal function tests. Patients with AF demonstrated significantly elevated levels of urea and creatinine, along with a slightly lower estimated glomerular filtration rate (eGFR). Elevated creatinine levels in heart failure often indicate impaired kidney function, while AF is a prevalent arrhythmia in patients with chronic kidney disease.[16,17] These might conclude that HFrEF with AF might have a higher incidence in developing kidney disorder than HFrEF with sinus rhythm. The left and right atrial diameters of patients with HFrEF and AF were considerably greater than those

of patients with sinus rhythm, according to the results of transthoracic echocardiography. AF and LA size are found to be correlated in both directions. When the mitral valve is closed, irregular atrial contractions can significantly raise LA pressure, which can ultimately result in left atrial enlargement (LAE). Consequently, LAE creates circumstances that raise the risk of AF development.[18]

Significant volume and pressure overload may be the cause of an increase in the size of the atria in the patients under study, which is especially pronounced in patients with AF. It is known that the main task of the LA is to ensure filling of the LV. This is achieved due to the alternation of the functional role of the LA, which acts during the cardiac cycle as an elastic reservoir, a passive conduit and an active pump (booster pump). Morpho functional restructuring leads to functional insufficiency of the LA, overload of the pulmonary circulation and the development of pulmonary hypertension, which is consistent with the results obtained.

It is believed that an increase in the size of the LV is associated with a worse prognosis and a lower probability of restoring lost cardiac function.[5] A large meta-analysis conducted in 2019 (14.939 patients with AF and 50.720 patients without AF) demonstrated strong associations between the diameter and volume of the LA and adverse events: HF decompensation and death. However, there were no differences in the end-diastolic volume, end-systolic volume of the left ventricle or LVEF between the groups in our study.

The results of the study should be considered taking into account the limitations of the echocardiography technique and the single-center nature of the study.

CONCLUSION

Patients with HFrEF and sinus rhythm more often had ischemic origin of cardiomyopathy, while in patients with HFrEF and AF had cardiomyopathy of dilated or mixed origin, which is confirmed by differences in sizes of atria and contractility index. The possible association of the obtained results with future adverse outcomes of HF requires further research.

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