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Heart Failure After Acute Coronary Syndrome: A Comprehensive Analysis from Bosnia and Herzegovina

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ABSTRACT

Background: The incidence of HF following ACS remains unacceptably high at discharge and several identified risk factors contribute to the development of HF in this context. **Objective:** This study investigated the prevalence and clinical significance of HF in patients admitted to the Clinic for Heart, Blood Vessels, and Rheumatic Diseases at the Clinical Center of the University of Sarajevo following ACS. **Methods**: This retrospective observational study was conducted at the Clinic for Heart, Blood Vessels, and Rheumatic Diseases of the Clinical Center of the University of Sarajevo between February 1st and April 1st, 2023, involving patients who were admitted because of ACS. **Results:** Patients with HFrEF were significantly (p=0.034) older (70.0 (62.0;76.0) vs 67.0 (57.5;75.0)), had (p=0.046) higher median score of LDH (321.5 (222.3; 501.5) vs. 256.0 (200.0; 420.0)), fibrinogen (p=0.047) (4.5 (3.2; 5.1) vs 3.6 (2.8; 5.0)), and NT-proBNP (p<0.001) (3705.0 (2500.0; 12559.5) vs. 500.0 (275.0; 333.0)), had enlarged left atrium diameter (3.9 (3.4; 4.4) vs 3.6 (3.1; 4.1)), enlarged left ventricular diameter both in diastole (5.1 (4.5; 5.8) vs 4.6 (4.1; 5.1)) and systole (3.7 (3.2; 4.1) vs 3.5 (3.1; 3.7)), thinner interventricular septum diameter both in diastole (1.1 (1.0; 1.2) vs 1.2 (1.1; 1.3)) and systole (1.3 (1.2; 1.5) vs. 1.4 (1.3; 1.5)) and elevated right ventricular systolic pressure (37.0 (30.0; 47.5) vs. 35.0 (28.0; 40.0)) compared to patients without HFrEF. Severe mitral regurgitation was more observed in group of patients with HFrEF (p<0.001). **Conclusion:** HFrEF patients showed a 40% incidence of post-ACS, had elevated LDH, fibrinogen, and NT-proBNP levels, along with distinct echocardiographic differences, including enlarged heart chambers and higher mitral regurgitation rates following ACS. Early HF risk factor management is crucial for optimizing outcomes in ACS patients.

Keywords. ACS, HFrEF, echocardiography, ventriculat function, heart diseases.

1. BACKGROUND

Despite significant advancements in the care of patients with acute coronary syndrome (ACS), the incidence of heart failure (HF) following ACS remains unacceptably high at discharge (1). Several identified risk factors contribute to the development of HF in this context. For instance, a recent prospective study highlighted that women have a notably higher risk of HF onset compared to men, even after adjusting for multiple variables (2). In addition, patients diagnosed with coronary artery disease (CAD) tend to be older and often present with a cluster of cardiovascular risk factors, including hypertension, diabetes, and obesity (3). These comorbidities collectively heighten the vulnerability of individuals with CAD to developing HF post-ACS. Furthermore, other studies have identified additional contributors to HF following ACS, such as the severity of coronary artery lesions, extent of myocardial damage, and presence of other cardiac complications (4). The persistence of high HF rates following ACS despite medical advancements underscores the need for targeted interventions addressing these risk factors and optimizing post-ACS care to reduce the burden of HF and improve patient

outcomes in this population (5, 6) .

2. OBJECTIVE

This study investigated the prevalence and clinical significance of heart failure in patients admitted to the Clinic for Heart, Blood Vessels, and Rheumatic Diseases at the Clinical Center of the University of Sarajevo following ACS. It compared demographic characteristics, cardiovascular risk factors, laboratory biomarkers, and echocardiographic parameters between patients with HF post-ACS, aiming to enhance understanding of HF phenotypes in this clinical context.

3. MATERIAL AND METHODS

This retrospective observational study was conducted at the Clinic for Heart, Blood Vessels, and Rheumatic Diseases of the Clinical Center of the University of Sarajevo. The study took place between February 1st and April 1st, 2023, involving patients who were admitted because of ACS. The study received approval from the Bioethical Committee of the Clinical Center of the University of Sarajevo and was conducted in accordance with all amendments of the Helsinki Declaration.

Subjects

The subjects included in the study were patients referred to the Clinic for Heart, Blood Vessels, and Rheumatic Diseases at the Clinical Center of the University of Sarajevo ACS and had undergone laboratory testing and cardiac echocardiographic imaging. The inclusion criteria were as follows: (i) patients with ACS, (ii) patients who underwent laboratory testing following ACS, and (iii) patients who underwent echocardiography following ACS. The exclusion criteria were as follows: (i) patients referred solely for coronary angiography from other healthcare institutions within the country, (ii) patients unwilling to provide informed consent, and (iii) patients who experienced mortality during PCI procedure. All subjects were informed about the study objectives, their voluntary participation, including informed consent, and the details of the data obtained for the study purposes.

Study instruments and data collection

All patients admitted to the Clinic for Heart, Blood Vessels, and Rheumatic Diseases at the Clinical Center of the University of Sarajevo for ACS underwent a comprehensive history analysis, which included assessing risk factors such as gender, age, hypertension, dyslipidemia, diabetes mellitus, smoking, and positive family history. Additionally, laboratory testing was conducted, encompassing a range of parameters including C-reactive protein, D-dimer, creatine kinase (CK), creatine kinase MB (CKMB), troponin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), urea, creatinine, fibrinogen, triglycerides, total cholesterol, low-density lipoprotein cholesterol (LDL-c), high-density lipoprotein cholesterol (HDL-c), very low-density lipoprotein cholesterol (VLDL-c), HbA1c, N-terminal pro-B-type natriuretic peptide (NT-proBNP), ferritin, total iron-binding capacity (TIBC), unsaturated iron-binding capacity (UIBC), and uric acid.

Furthermore, all patients underwent transthoracic echocardiography using a GE VividTM S70 ultrasound machine. The echocardiographic studies were recorded and analyzed by multiple experts to ensure objectivity in the analysis. Various echocardiography parameters related to left ventricular (LV) function and hemodynamic status were measured, including left atrium diameter (LA), left ventricular end-diastolic diameter (LVEDD), left ventricular end-systolic diameter (LVEDS), interventricular septum diastolic diameter (IVSD), interventricular septum systolic diameter (IVSS), right ventricular systolic pressure (RVSP), presence of mitral valve regurgitation (MR), aortic valve regurgitation (AR), tricuspid valve regurgitation (TR), mitral valve stenosis (MS), aortic valve stenosis (AS), left ventricular ejection fraction (LVEF), and the presence of pericardial effusion. Based on global systolic function, patients were categorized into three groups: HFrEF, consisting of patients with LVEF < 40%, HFmrEF consisting of patients with LVEF 41-49%, and those with HFpEF consisting of patients with LVEF > 50%,

Statistical analysis

The gathered data was condensed and analyzed using descriptive statistics. For normally distributed data, frequencies and percentages were used to present the data (mean ± standard deviation). For data that did not follow a normal distribution, the median along with the 25th and 75th percentiles were reported. To

Variables		Without HFreF N=129	HFrEF N=83	Total N=212	p-value
Sex (No, %)	Male	91 (70.5)	64 (77.1)	155 (73.1)	0.293
	Female	38 (29.5)	19 (22.9)	57 (26.9)	
Age (median, 25th, 75th percentile)		67.0 (57.5;75.0)	70.0 (62.0;76.0)	68.0 (60.0; 75.0)	0.034
Risk factors (No, %)	Hypertension	70 (54.3)	47 (56.6)	117 (55.8)	0.735
	Diabetes mellitus	36 (27.9)	22 (26.5)	58 (27.3)	0.939
	Dislipidemia	69 (53.5)	42 (50.6)	111 (52.3)	0.374
	Smoking	50 (38.8)	26 (31.3)	76 (35.8)	0.216
	Positive family history for CVD	63 (48.8)	38 (45.8)	101 (47.6)	0.663
	Previous ICV	10 (7.8)	9 (10.8)	19 (8.9)	0.488
	Renal inssufi-cency	14 (10.8)	8 (9.6)	22 (10.3)	0.981

Table 1. Sex, age and cardiovascular associated risk factors such as hypertension, diabetes mellitus, hyperlipidemia, smoking status, positive family history of cardiovascular disease, previous cerebrovascular insults and renal insufficiency between patients with and without HFreF admitted at the Clinic for Heart, Blood Vessels and Rheumatic Diseases of Clinical Center of University of Sarajevo

examine the relationship between different variables and specific phenomena, independent samples t-tests, Mann-Whitney U tests, or chi-squared tests were performed based on the nature of the data. A statistical significance level of $p < 0.05$ (two-sided) was applied.

4. RESULTS

In total 212 patients from the Clinic for Heart, Blood Vessels and Rheumatic Diseases of Clinical Center of University of Sarajevo were included in the study. Our patients were predominantely male 155 (72.4%), with a median age of 68.0 (60.0; 75.0), having hypertension 117 (55.8%), diabetes mellitus 58 (27.3%), dislipidemia 111 (52.3%), were active smokers 76 (35.8%) and had family history of cardiovascular diseases 101 (47.6%). The sample included 83 (39.1%) patients with HFrEF and 129 (60.9%) without HFrEF following ACS. No statistical difference ($p>0.05$) regarding sex and cardiovascular risk factors between patients with HFrEF and without HFrEF was observed. However, patients with HFrEF were significantly (U=4428.0, p=0.034) older (70.0 (62.0;76.0)) compared to patients without HFrEF (67.0 (57.5;75.0)) following ACS. All other data regarding sex, age and cardiovascular associated risk factors such as hypertension, diabetes mellitus, hyperlipidemia, smoking status, positive family history of cardiovascular disease, previous cerebrovascular insults and renal insufficiency between patients with and without HFreF are presented in Table 1.

		Without HFreF N=129	HFrEF N=83	p-value
Laboratory findings median (25th, 75th percentile)	C-reactive protein	5.7 (2.9; 15.5)	7.3 (2.4; 25.3)	0.264
	D-dimer	0.6 (0.3; 1.1)	0.8 (0.4; 1.6)	0.346
	AST	33.0 (26.0; 57.0)	36.0 (24.0; 74.0)	0.762
	ALT	32.5 (26.0; 49.8)	39.0 (22.3; 59.0)	0.470
	CK	166.0 (89.3; 441.0)	146.0 (64.8; 400.8)	0.239
	CKMB	37.0 (22.0; 60.0)	40.0 (23.0; 116.0)	0.518
	Troponin	395.5 (67.5; 1166.8)	290.0 (90.3; 1453.3)	0.655
	LDH	256.0 (200.0; 420.0)	321.5 (222.3; 501.5)	0.046
	Fibrinogen	3.6 (2.8; 5.0)	4.5 (3.2; 5.1)	0.047
	Urea	5.5 (4.3; 9.1)	6.6 (5.0; 10.2)	0.126
	Creatinine	84.0 (71.5; 120.0)	89.0 (73.5; 110.5)	0.689
	Tryglicerides	1.56 (1.2; 2.5)	1.54 (1.1; 2.2)	0.547
	Total cholesterol	5.1 (4.0; 5.7)	4.6 (3.5; 5.7)	0.167
	HDL-c	1.0 (0.9; 1.3)	1.0 (0.8; 1.3)	0.494
	LDL-c	3.5 (2.5; 4.5)	3.1 (2.2; 4.6)	0.689
	VLDL-c	0.6 (0.5; 1.0)	0.6 (0.4; 1.0)	0.809
	NT-proBNP	500.0 (275.0; 333.0)	3705.0 (2500.0; 12559.5)	<0.001
	Hb1Ac	6.3 (5.4; 7.2)	5.8 (5.7; 6.7)	0.574
	Ferritin	230.0 (224.0; 333.0)	265.9 (225.8; 543.5)	0.129
	TIBC	45.0 (36.0; 46.1)	45.6 (42.3; 49.0)	0.292
	UIBC	30.1 (25.3; 35.0)	33.1 (28.1; 39.7)	0.444
	Uric acid	445.0 (354.0; 524.5)	421.0 (339.0; 580.0)	0.962

Table 2. Laboratory findings between patients with and without HFreF admitted at the Clinic for Heart, Blood Vessels and Rheumatic Diseases of Clinical Center of University of Sarajevo

Patients were admitted to the Clinic for Heart, Blood Vessels and Rheumatic Diseases of Clinical Center of University of Sarajevo because of ACS 212 (100.0%). On the laboratory report, HFrEF patients had a significantly (p=0.046) higher median score of LDH (321.5 (222.3; 501.5) vs. 256.0 (200.0; 420.0)), fibrinogen (p=0.047) (4.5 (3.2; 5.1) vs 3.6 (2.8; 5.0)), and NT-proBNP (p<0.001) (3705.0 (2500.0; 12559.5) vs. 500.0 (275.0; 333.0)) when compared to patients without HFrEF. All other laboratory report findings between patients with and without HFreF are presented in Table 2.

All patients admitted to the Clinic for Heart, Blood Vessels and Rheumatic Diseases of Clinical Center of University of Sarajevo have undergone echocardiographical examination. All 2D echocardiography findings among between patients with and without HFreF are

			Without HFreF N=129	HFrEF N=83	p-value
Echo findings	LA		3.6 (3.1; 4.1)	3.9 (3.4; 4.4)	0.006
	LVEDD		4.6 (4.1; 5.1)	5.1 (4.5; 5.8)	<0.001
	LVEDS		3.5 (3.1; 3.7)	3.7 (3.2; 4.1)	0.005
	IVSD		1.2 (1.1; 1.3)	1.1 (1.0; 1.2)	0.017
	IVSS		1.4 (1.3; 1.5)	1.3 (1.2; 1.5)	0.050
	RVSP		35.0 (28.0; 40.0)	37.0 (30.0; 47.5)	0.049
	MR				
		Mild	71 (55.0)	32 (38.6)	<0.001
		Moderate	50 (38.7)	28 (33.7)	
		Severe	8 (6.3)	23 (27.7)	
	AR				
		Mild	91 (70.5)	51 (61.4)	0.376
		Moderate	35 (27.1)	30 (36.1)	
		Severe	3 (2.4)	2 (2.5)	
	TR				
		Mild	83 (64.3)	40 (48.2)	0.060
		Moderate	41 (31.8)	37 (44.6)	
		Severe	5 (3.9)	6 (7.2)	

Table 3. 2D echocardiography findings between patients with and without HFreF admitted at the Clinic for Heart, Blood Vessels and Rheumatic Diseases of Clinical Center of University of Sarajevo. LA-left atrium diameter, LVEDD-Left ventricular end diastolic diameter, LVEDS-left ventricular end systolic diameter, IVSD-interventricular septum diastolic diameter, IVSS-interventricular septum systolic diameter, RVSP-right ventricular systolic pressure, MR-mitral valve regurgitation, AR- aortic valve regurgitation, TR-tricuspid valve regurgitation,

presented in Table 3. HFrEF patients had enlarged left atrium diameter (3.9 (3.4; 4.4) vs 3.6 (3.1; 4.1)), enlarged left ventricular diameter both in diastole (5.1 (4.5; 5.8) vs 4.6 (4.1; 5.1)) and systole (3.7 (3.2; 4.1) vs 3.5 (3.1; 3.7)), thinner interventricular septum diameter both in diastole (1.1 (1.0; 1.2) vs 1.2 (1.1; 1.3)) and systole (1.3 (1.2; 1.5) vs. 1.4 (1.3; 1.5)) and elevated right ventricular systolic pressure (37.0 (30.0; 47.5) vs. 35.0 (28.0; 40.0)). Severe mitral regurgitation was more observed in group of patients with HFrEF ($p<0.001$).

5. DISCUSSION

To the best of our knowledge, this study represents one of the initial investigations in Bosnia and Herzegovina focusing on HFrEF following ACS. Our patient cohort was predominantly male, older, and exhibited prevalent risk factors such as hypertension, diabetes mellitus, and dyslipidemia. Notably, 40% of the patients experienced HFrEF following ACS during the observed period. Those with HFrEF were notably older compared to individuals without HFrEF post-ACS. Laboratory analyses indicated that HFrEF patients had elevated levels of LDH, fibrinogen, and NT-proBNP compared to their non-HFrEF counterparts. Additionally, echocardiography revealed distinct structural differences in cardiac parameters among HFrEF patients, including enlarged left atrium and ventricular diameters, thinner interventricular septum, and higher right ventricular systolic pressure, along with a higher prevalence of severe mitral regurgitation. These findings emphasize the critical importance of early identification and management of HF risk factors in ACS patients to optimize clinical outcomes and customize treatment approaches.

When compared to similar studies investigating HFrEF following ACS, older patients exhibited a substantially heightened risk, up to six times greater after hospital discharge (4, 7). This increased vulnerability is likely due to delayed presentation or diagnosis (8), diminished functional reserve and adaptive capacity (9), a greater burden of comorbidities, and age-related physiological alterations. Age-related changes in cardiac structure and function (9), such as decreased myocardial contractility and vascular compliance, may also contribute to the elevated risk of HF in this population.

Our laboratory findings also correlate with similar studies (10, 11), which demonstrated higher levels of LDH among patients with HF. Elevated LDH levels can indicate tissue damage and cellular breakdown, commonly observed in HF due to impaired cardiac function and insufficient oxygen delivery to tissues. LDH is an enzyme found in various tissues, and its elevation in HF reflects the underlying pathological processes, including myocardial injury and cellular stress (11). This marker is useful in assessing disease severity and prognosis in patients with HF. Additionally, our study observed elevated fibrinogen levels in patients with HFrEF, which aligns with findings from similar research (12) and could be attributed to inflammation, procoagulation, and increased blood viscosity in the development of early myocardial dysfunction. Lastly, NT-proBNP levels were higher among patients with HFrEF compared to those without, which aligns with a study from the Netherlands (13).

When assessing the echocardiographic characteristics of HFrEF patients, our study observed enlarged left atrium and ventricular diameters, along with a thinner interventricular septum and higher right ventricular systolic pressure. The dilation of the left atrium and ventricle represents a response to increased volume or pressure and alterations in the heart's architecture (14). Elevated right ventricular systolic pressure indicates increased pressure in the right side of the heart, potentially resulting from left HF (15). Additionally, we observed also a higher incidence of severe mitral regurgitation in HFrEF patients which further contributes to HF (16). In these cases, mitral regurgitation in HFrEF can result from structural changes in the heart, such as left ventricular dilation and dysfunction, which affect the function of the mitral valve.

6. CONCLUSION

This study in Bosnia and Herzegovina focused on HFrEF after ACS. The patient cohort, predominantly older males with prevalent risk factors like hypertension and diabetes, showed a 40% incidence of HFrEF post-ACS. HFrEF patients had elevated LDH, fibrinogen, and NT-proBNP levels, along with distinct echocardiographic differences, including enlarged heart chambers and higher mitral regurgitation rates. Early HF risk factor management is crucial for optimizing outcomes in ACS patients.

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