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Patterns of heart failure patients – Data from a single East-European centre

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ABSTRACT

Objectives. *The present study aims to describe the clinical and biological profile of heart failure patients from central Romania.*

Material and method. *A single centre-based retrospective, observational, descriptive study involving heart failure patients admitted from January 2018 to March 2020 was conducted. Only patients who had echocardiographic data determined by the same examiner were included. Patients were classified according to LVEF at admission in three subgroups: preserved LVEF subgroup (HFpEF, LVEF ≥ 50%), moderate LVEF subgroup (HFmrEF, LVEF 40-49%), reduced LVEF subgroup (HFrEF, LVEF < 40%) and their clinical and biological profile was assessed. Comorbidities were recorded using the Charlson comorbidity index (CCI).*

Outcomes. *A total of 175 patients (57.7% males) were included in our study, with a mean age of 65.3 ± 11.7 years. 44% of patients had more than one hospital admission during the studied timeframe. Mean calculated left ventricular ejection fraction was 47.1% ± 12.1%. According to LVEF 62.8% of patients were in HFpEF group, 20.5% in the HFrEF group and 16.5% in the HFmrEF group. Dyspnoea was the most common presenting symptom in 65.7% of patients, being accompanied by fatigue in majority of cases (63.4%). Charlson comorbidity index mean value for the study population was 4.6 ± 2.1, 4.6 ± 2 in the HFpEF group, 5.2 ± 1.9 in the HFmrEF group and 4.03 ± 2.2 in the HFrEF group. Arterial hypertension was the most frequent comorbid condition and risk factor at the same time, in both men and women.*

Conclusions. *The clinical and biological profile of the heart failure patients is complex, diverse and further research is needed for improving therapeutic and follow-up management of these patients.*

Keywords: heart failure, clinical profile, Charlson comorbidity index

INTRODUCTION

Heart failure (HF) is a debilitating clinical syndrome characterized by typical symptoms and signs caused by a structural and/or functional cardiac abnormality, resulting in a reduced cardiac output and/or elevated intra-cardiac pressures at rest or during stress (1). In developed countries, the prevalence of HF is approximately 1-2% of the adult population, rising to ≥10% among people > 70 years of age (2-5). HF high mortality rates are comparable to those of various malignancies, the 5-year mortality reaching almost 50% (1,6,7).

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Due to it's complexity, HF is a major burden for public health, being the main cause for hospitalization, re-hospitalization and outpatient visits (8). Heart failure patients often experience a considerable number of comorbid conditions, which further affect the disease management and prognostic (9). Ischemic heart disease, hypertension (HT), diabetes, dyslipidaemia and smoking also represent risk factors for developing HF. It is estimated that approximately 7-8 years after an acute coronary syndrome, one third of patients will eventually develop heart failure (10). The lifetime risk for developing heart failure increases in the presence of a history of myocardial infarction in both men and women (11). Hypertension associated risk of HF is smaller comparative to that associated with myocardial infarction. However, HT has a greater prevalence, therefore contributes more to the burden caused by HF (2). The presence of diabetes and insulin resistance is of major importance in HF development; diabetes itself increases the risk nearly as much as the presence of three other atherosclerotic risk factors (12). Cardiovascular disease risk factors, including dyslipidaemia in the form of increased ratio of total cholesterol to HDL cholesterol (13), smoking and obesity commonly precede the onset of heart failure, regardless of left ventricular ejection fraction (LVEF) (14).

To date, many studies have assessed the characteristics of heart failure in patients from different regions (15-17). Our study aims to describe a regional, clinical and biological profile of heart failure patients.

MATERIAL AND METHODS

A single centre-based, retrospective, observational, descriptive, non-interventional study involving 175 heart failure patients admitted to Targu Mures Emergency County Hospital, Internal Medicine Clinic II, Cardiology Department, from January 2018 to March 2020 was conducted. The inclusion criteria consisted in new-onset or worsening HF diagnosis according to European Society of Cardiology (ESC) 2016 Guidelines for the diagnosis and treatment of acute and chronic heart failure, age > 18 years, irrespectively of comorbidities, and informed consent of the patients. To minimalize inter-observer variability (18), we only included patients who had echocardiographic data determined by the same examiner. The exclusion criterion was represented by lack of informed consent.

Patient's data were collected from electronic and paper-based recordings and the following variables were analysed: age, gender, environment, risk factors, type of admission, length of hospitalization, medical history, body mass index (BMI), NYHA classification, presenting symptoms, blood pressure and heart rate, electrocardiogram and transthoracic echocardiography measurements. Laboratory data included complete blood count, renal tests, serum iron, fasting blood sugar, serum uric acid, serum electrolytes, lipid profile and natriuretic peptides (NT-proBNP). Comorbidities were recorded using the Charlson comorbidity index (CCI), the most widely used index for 10-year survival prediction, validated in both clinical and surgical patients (19). The equation used for the calculation of 10-year survival rate was: 10-year survival = 0.983^ [e^ (CCI x 0.9)], e = Euler's constant.

Furthermore patients were subclassified according to LVEF at admission in three subgroups: preserved LVEF subgroup (HFpEF, LVEF ≥ 50%), moderate LVEF subgroup (HFmrEF, LVEF 40-49%), reduced LVEF subgroup (HFrEF, LVEF < 40%) and analysed their clinical and biological profile.

Transthoracic cardiac ultrasound was performed using a Philips Vivid E9 System (GE Vingmed Ultrasound AS, Norway) and the left ventricle ejection fraction (LVEF) was determined for each patient. For the electrocardiographic assessment, a BTL-08 Plus System (BTL Industries, Hertfordshire, Great Britain) was used. Laboratory investigations were performed with automatic systems Sysmex XS-1000i (Sysmex Europe GmbH, Norderstedt, Germany) and Konelab Prime 60i (Thero Fisher Scientific, Waltham, SUA). For the assessment of renal function, estimated glomerular filtration rate was calculated using CKD-EPI Creatinine 2009 equation.

Statistical analysis was performed using Microsoft®Excel®2018 (Microsoft Corporation, Redmond, WA, USA) and GraphPad Software (GraphPad Prism version 8.00 for Windows 64-bit, GraphPad Software, La Jolla California, USA). Categorical data are presented as frequencies (percentages) and continuous data are presented as the mean values ± standard deviation (SD). Our work fulfils the international regulations stated in the Declaration of Helsinki and was approved by the Local Ethics Committee.

RESULTS

Our studied group included 175 patients (57.7% males) diagnosed with heart failure according to 2016 ESC Guidelines, with a mean age of 65.3 ± 11.7 years. The male/female ratio was 1:1 in HFpEF group, 2.6:1 in HFmrEF and 2.2:1 in HFrEF group. 44% of patients had more than one hospital admission during the studied timeframe, with an average hospitalization length of 7.2±3.3 days. At admission, 62.8% of patients presented NYHA I or II clinical symptoms, 32.6% NYHA III and 4.6% manifested a more severe exacerbation of the disease with NYHA IV symptoms. Mean systolic and diastolic blood pressure at admission were 128.1 ± 18.9 mmHg and 78.1 ± 10.9 mmHg respectively. Dyspnoea

was the most common presenting symptom in 65.7% of patients, being accompanied by fatigue in majority of cases (63.4%). 33.1% of patients complained of chest pain, 28.5% of palpitations and 13.7% of lower limbs oedema. Symptoms like cough (8%), oscillating blood pressure values (11.4%), dizziness (5.7%), headache (5.1%), claudication (4.5%), unintentional weight loss (4%) and syncope (1.7%) were also present but did not represent main causes for admission.

The common risk factors involved in heart failure development were identified in our study population, with the highest prevalence represented by HT (76.5% of patients having a medical history of HT at admission), followed by chronic coronary syndrome (49.1%), atrial fibrillation (46.2%), obesity (40.5%), dyslipidaemia (42.8%) and diabetes mellitus (22.8%).

After reviewing patient's medical history, the Charlson comorbidity index (CCI) was calculated for each patient and the mean value for the study population was 4.6 ± 2.1. According to the LVEF, CCI means were 4.6 ± 2 in the HFpEF group, 5.2 ± 1.9 in the HFmrEF group and 4.03 ± 2.2 in the HFrEF group. Comorbid conditions of heart failure patients included in our study are presented in Table 1.

Transthoracic echocardiography was performed at admission or in the first 48 hours for the majority of patients; mean calculated LVEF was 47.1% ± 12.1%. 62.8% of patients were documented as having HFpEF, 20.5% HFrEF and 16.5% HFmEF. In the reduced LVEF group, 6% presented NYHA IV symptoms, while 78.1% of patients were included in NYHA I or II class and had a preserved LVEF. Valvular heart disease (62.3% males and 68.9% females) and chronic kidney disease (60.3% males and 81% females) are the next most frequent comorbidities. Demographic, baseline clinical and biological characteristics of HF patients according to their LVEF are presented in Table 2 and Table 3.

DISCUSSIONS

The present study includes 175 patients diagnosed with heart failure admitted to our County's Hospital Cardiology ward. To date, there are numerous studies describing heart failure patterns including a similar number of patients. For example, a recent study from Sokolska et al. including 137 patients describes onset dyspnea patterns in acute HF patients (20). Similar to it, Nowak et al. describe acute HF phenotypes in the emergency department analyzing 127 patients (21). The mean ages of the patients included in the aforementioned studies (65 ± 13 and 70 ± 15.5 years, respectively) are comparable to ours (65.3 ± 11.7 years),

TABLE 1. *Comorbid conditions of the studied population. CVA or TIA – cerebrovascular accident or transient ischemic attack. COPD – chronic obstructive pulmonary disease. DCM – dilated cardiomyopathy. N – number of patients, % – percentage*

Comorbidities	Overall (N = 175), (N, %)	Male (N = 101), (N, %)	Female (N = 74), (N, %)
Arterial hypertension	134 (76.5%)	73 (72.2%)	61 (82.4%)
Chronic kidney disease	121 (69.1%)	61 (60.3%)	60 (81%)
Valvular heart disease	114 (65.1%)	63 (62.3%)	51 (68.9%)
Pulmonary hypertension	94 (53.7%)	51 (50.4%)	43 (58.1%)
Chronic coronary syndrome	86 (49.1%)	49 (49.4%)	37 (50%)
Atrial fibrillation	81 (46.2%)	40 (39.6%)	41 (55.4%)
Obesity	71 (40.5%)	34 (33.66%)	37 (50.0%)
Hypercholesterolemia	50 (28.5%)	23 (22.7%)	27 (36.4%)
Myocardial infarction	44 (25.1%)	33 (32.6%)	11 (14.8%)
Anaemia	42 (24.0%)	20 (19.8%)	22 (29.7%)
Hyperuricemia	41 (23.4%)	17 (16.8%)	24 (32.4%)
Diabetes mellitus	40 (22.8%)	23 (22.7%)	17 (22.9%)
Hypertriglyceridemia	25 (14.2%)	15 (14.8%)	10 (13.5%)
DCM	24 (13.7%)	17 (16.8%)	7 (9.4%)
CVA or TIA	20 (11.4%)	13 (12.8%)	7 (9.4%)
Peripheral vascular disease	16 (9.1%)	15 (14.8%)	1 (1.3%)
Thyroid dysfunction	16 (9.1%)	3 (2.9%)	13 (17.5%)
COPD	16 (9.1%)	11 (10.8%)	5 (6.7%)
Localized solid tumour	6 (3.4%)	4 (3.9%)	2 (2.7%)
Metastatic solid tumour	5 (2.8%)	2 (1.9%)	3 (4.0%)
Liver disease	5 (2.8%)	3 (2.9%)	2 (2.7%)
Peptic ulcer disease	2 (1.1%)	1 (0.9%)	1 (1.3%)
Dementia	2 (1.1%)	1 (0.9%)	1 (1.3%)

TABLE 2. *Demographic and baseline clinical characteristics of HF patients according to their LVEF. HFpEF – heart failure with preserved ejection fraction, HFmEF – heart failure with moderate ejection fraction, HFrEF – heart failure with reduced ejection fraction, BMI – body mass index, SBP – systolic blood pressure, DBP – diastolic blood pressure, SD – standard deviation, N – number of patients*

Characteristic	Overall (N = 175)	HFpEF (N = 110)	HFmEF (N = 29)	HFrEF (N = 36)
Age, years (mean ± SD) (min-max)	65.3 ± 11.7 (31-90)	66.3 ± 11.1 (31-89)	67.5 ± 10.6 (47-90)	60.4 ± 13.0 (34-83)
Gender (N, %) Male Female	 101 (57.7%) 74 (42.3%)	 55 (50.0%) 55 (50.0%)	 21 (72.4%) 8 (27.5%)	 25 (69.4%) 11 (30.5%)
Urban setting (N, %)	85 (48.5%)	52 (47.2%)	17 (58.6%)	16 (44.4%)
BMI (kg/m^2) mean ± SD) (min-max)	29.2 ± 5.4 (17.4-51.5)	29.3 ± 5.0 (17.4-45.1)	29.6 ± 5.9 (20.4-51.5)	28.5 ± 6.2 (19.8-48.0)
NYHA functional class, (N, %) ≤II III IV	 110 (62.8%) 57 (32.6%) 8 (4.6%)	 86 (78.1%) 23 (20.9%) 1 (0.9%)	 12 (41.3%) 16 (55.1%) 1 (3.4%)	 12 (33.3%) 18 (50%) 6 (16.6%)
SBP (mmHg), (mean ± SD) (min-max)	128.1 ± 18.9 (80-210)	131 ± 18 (80–210)	125 ± 15 (95–160)	121 ± 20 (80–160)
DBP (mmHg), (mean ± SD) (min-max)	78.1 ± 10.9 (50-110)	79.2 ± 9.9 (50-110)	77.4 ± 11.4 (55-100)	75.1 ± 11.1 (55-100)
Heart rate (beats/min) (mean ± SD) (min-max)	75.2 ± 18.1 (40-188)	73.3 ± 15.7 (48-120)	74.5 ± 18.1 (40-114)	81.8 ± 23.4 (54-188)
Risk factors (N, %) Diabetes mellitus Arterial hypertension Obesity Hypercholesterolemia Hypertriglyceridemia	 40 (22.8%) 134 (76.5%) 71 (40.5%) 50 (28.5%) 25 (14.2%)	 25 (22.7%) 96 (87.2%) 46 (41.8%) 36 (32.7%) 14 (12.7%)	 8 (27.5%) 22 (75.8%) 12 (41.3%) 7 (24.1%) 5 (17.2%)	 7 (19.4%) 16 (44.4%) 12 (33.3%) 7 (19.4%) 6 (16.6%)
Deaths (N, %)	1 (0.5%)	1 (1.1 %)	0 (0%)	0 (0%)

TABLE 3. *Baseline biological characteristics of HF patients according to their LVEF. HFpEF – heart failure with preserved ejection fraction, HFmEF – heart failure with moderate ejection fraction, HFrEF – heart failure with reduced ejection fraction, NT-proBNP - N-terminal pro-brain natriuretic peptide, eGFR – estimated glomerular filtration rate, N – number of patients*

Laboratory findings (units, range)	Overall (N=175)	HFpEF (N=110)	HFmEF (N=29)	HFrEF (N=36)
NT-proBNP (pg/ml, < 125 pg/ml)	2252 ± 2968.8 (58-13959)	1612 ± 2923.6 (58-12614)	1654 ± 181.1 (71-6371)	2314 ± 3441.0 (197-13959)
Creatinine (mg/dl, 0.7-1.2 mg/dl)	1.1 ± 0.7 (0.5-8.0)	1.0 ± 1.1 (0.5-4.4)	1.6 ± 1.5 (0.6-8.0)	1.1 ± 0.4 (0.7-2.9)
eGFR (ml/min/1.73 m^2, >90 ml/min/1.73 m^2)	71.9 ± 26.0 (5.4-128.9)	73.6 ± 24.6 (13.8-124.2)	62.9 ± 31.0 (5.4-127.1)	74.8 ± 24.6 (22.4-129.9)
Hemoglobin (g/dl, 13-17 g/dl)	13.5 ± 1.8 (5.5-17.8)	13.6 ± 2.82 (5.5-17)	13.0 ± 2.2 (6.2-17)	13.5 ± 1.9 (8.1-17.8)
Platelets (x 103 /µl, 150-400 x 103 /µl	231.0 ± 67.4 (51.0-486.0)	235.3 ± 62.6 (51.0-433.0)	219.8 ± 82.3 (84.0-486.0)	227.3 ± 69.6 (95.0-388.0)
Serum iron (µmol/l, 9.0-30.4 µmol/l)	15.1 ± 7.6 (3.3-54.8)	14.0 ± 5.9 (3.3-44.4)	16.2 ± 10.0 (3.8-54.8)	17.6 ± 9.5 (4.9-45.3)
Blood glucose (mg/dl, 70-105 mg/dl)	110 ± 29.2 (61.7-329.7)	109.7 ± 29.3 (79.3-329.7)	109 ± 21.6 (82.6-163.3)	111.5 ± 34.2 (61.7-244.4)
Urea (mg/dl, 15-46 mg/dl)	60.8 ± 65.4 (13.2-570.5)	53.7 ± 55.8 (13.2-532.1)	55.2 ± 24.5 (23.0-108.1)	83.8 ± 98.5 (21.3-570.5)
Uric acid (µmol/l, 200-400 µmol/l)	326.9 ± 112.1 (83-885)	308.0 ± 109.4 (83-837)	352.5 ± 90.8 (188-563)	366.2 ± 124.4 (206-885)
Sodium (mmol/l, 136-145 mmol/l)	141 ± 4.0 (125-150)	141.6 ± 3.6 (127-150)	140 ± 3.8 (130-150)	139.4 ± 4.8 (125-147)
Potassium (mmol/l, 3.5-5.1 mmol/l)	4.3 ± 0.5 (2.9-5.8)	4.2 ± 0.4 (2.9-5.7)	4.6 ± 0.4 (3.8-5.5)	4.3 ± 0.5 (3.4-5.8)
Total cholesterol (mg/dl, 110-200 mg/dl)	172.5 ± 47.7 (63.4-322.1)	180.6 ± 18.9 (79.6-322.1)	158.5 ± 46.6 (81.2-292.7)	159.3 ± 49.7 (63.4-292.3)
Triglycerides (mg/dl, 50-170 mg/dl)	126.2 ± 59.0 (25.6-364.0)	124.4 ± 56.2 (25.6-278.1)	118.8 ± 56.3 (33.6-273.6)	137.3 ± 68.6 (51.3-364.0)

with a male predominance (80% and 52%, respectively) which is also found in our study (57.7%). 62.8% of patients presented mild clinical symptoms at admission, classified as NYHA I or II. This could be due to the fact that only 12.5% of the patients were first addressed to the Emergency Department. Although 76.5% of patients had a history of hypertension, mean systolic and diastolic blood pressures at admission where relatively normal range, maybe reflecting a good adherence to antihypertensive medication of this category of patients. Numerous studies described dyspnea as the major complaint of HF patients (20,22). Our results are in line with these findings, 65.7% of our patients presenting dyspnea as the main cause for hospital admission. Almost as common, fatigue was present in 63.4% of patients, followed by chest pain, palpitations and lower limbs edema. In a study by Farmakis et al. (22) along with dyspnea (73.4%), 43.8% of patients presented fatigue, 42.7% presented peripheral edema and 27.9% reported weight gain. Opposite to this finding, in our study 4% of patients reported unintentional weight loss. These results support the involvement of different mechanisms of the disease either in weight gain through water retention, or weight loss in advanced heart failure.

In heart failure patients, a plethora of comorbid conditions may be identified. Our results show that hypertension is the most frequent comorbid condition and risk factor at the same time, in both men and women. A history of myocardial infarction was identified in 32.6% of males and 14.8% of female patients (25.1% of the entire studied population). Nowak et al. (21) reported hypertension as the most frequent comorbidity in their patients (79%) and diabetes mellitus second most frequent (52%). A history of myocardial infarction was identified in 34% of patients, while CKD was present in only 43% of patients compared to our study (69.1%). Diabetes mellitus was identified in less than 23% of patients, similar to the above-mentioned study by Sokolska et al (20).

The CCI mean value in our patients was 4.6 ± 2.1. Interestingly, in the HFrEF subgroup the mean CCI was 4.03 ± 2.2, while in the HFpEF group the mean was 4.6 ± 2. Thus, the HFrEF group may have a better 10-year survival rate (52.4%) than the HFpEF group (34.0%). This could owe to the fact that HF patients with a reduced ejection fraction benefit from better implemented therapy strategies and follow-up that the other categories. Although controversial, similar results were obtained by other studies as well (23).

When we indexed patients according to their LVEF, 62.8% were in HFpEF group, 20.5% in the HFrEF group and 16.5% in the HFmrEF group. A different percentage was reported in a study (22) comprising 3,257 patients of whom 22.9% had a LVEF ≥ 50%, 24.9% had a LVEF between 40-49% and in 52.1% of patients the LVEF had values < 40%. Mean systolic and diastolic blood pressures tend to decrease with the LVEF (131 ± 18 and 79.2 ± 9.9; 125 ± 15 and 77.4 ± 11.4; 121 ± 20 and 75.1 ± 11.1), while heart rate values increase (73.3 ± 15.7; 74.5 ± 18.1 and 81.8 ± 23.8). A study by Gök et al. (24) found comparative results: in patients aged 65-79 years mean SBP was 103 ± 36 mmHg in HFrEF group, 114 ± 22 mmHg in HFmrEF group and 120 ± 14 mmHg in the HFpEF group. In elderly patients (aged > 80 years) accordingly to EF values, SBP values were 92 ± 48 mmHg, 115 ± 23 and 113 ± 19 respectively. The mean heart rate values were directly proportional with the mean SBP and LVEF in both age groups (69 ± 24, 76 ± 12 and 79 ± 13 in patients aged 65-79 years; 64 ± 31, 77 ± 16 and 78 ± 16 in patients > 80 years).

Study limitations

Registered data were based only on the diagnostic coding of the hospital and patient's medical history, which depended on the accuracy and integrity of the documentation. Another issue is related to a relative small number of cases admitted in a single centre, thus more data should be added in order to obtain a more precise pattern of heart failure patients.

CONCLUSIONS

Heart failure patients express multifaceted clinical and biological profiles pointed in various HF trials. The observed discrepancies could be due to trial-specific issues, country differences, patient characteristics, outcomes and treatment effect heterogeneity. Further research into characterizing HF patients is mandatory for improving therapeutic and follow-up management of these patients.

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