ORIGINAL ARTICLE

Epidemiology and clinical characteristics of hospitalized patients with heart failure with reduced, mildly reduced, and preserved ejection fraction

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KEY WORDS

clinical characteristics, comorbidities, heart failure phenotypes

ABSTRACT

INTRODUCTION There is still little information regarding a detailed description and predictors of different subtypes of heart failure (HF) in the Polish population.

OBJECTIVES This study sought to characterize the differences between hospitalized patients with HF divided into HF with preserved ejection fraction (HFpEF; EF ≥50%), mildly reduced EF (HFmrEF; EF 40%–49%), and reduced EF (HFrEF; EF <40%), and to identify factors related to each HF subtype.

PATIENTS AND METHODS Patients from the hospital database whose hospitalization was coded as HF-related between 2014 and 2019 were included in the analysis.

RESULTS A total of 2601 patients were included, of whom 62% had HFrEF, 13% had HFmrEF, and 25% had HFpEF. The patients with HFpEF, as compared with those with HFrEF and HFmrEF, were older (70.5 vs 61.6 vs 66.5 years, P <0.001), less often male (44% vs 68.3% vs 81.3%, P <0.001), and less likely to have an ischemic etiology of HF (19.3% vs 49.8% vs 34.4%, P <0.001) but they were more likely to have hypertension (87.3% vs 78.2% vs 78.2%, P <0.001), atrial fibrillation (64.5% vs 55.6% vs 59.5%, P <0.001), cancer (32.2% vs 19.6% vs 28.7%; P <0.001), and anemia (25.5% vs 15.9% vs 20.5%, P <0.001). Of 3 multivariable models, the one predicting HFpEF was the strongest (P <0.001, area under the curve, 0.79), and included age, sex, aortic stenosis, hypertension, anemia, cancer, thyroid abnormality, atrial fibrillation, longer history of HF, ischemic etiology, coronary artery disease, diabetes mellitus, and liver failure.

CONCLUSIONS HFrEF and HFpEF differed significantly in terms of baseline characteristics, while HFmrEF was in the middle of the HF spectrum, tending to be a mixture of HFpEF and HFrEF characteristics.

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INTRODUCTION Heart failure (HF) is a complex clinical syndrome associated with significant morbidity and mortality.[1] Despite improvements in the prognosis of patients with HF due to the implementation of pharmacologic and invasive therapies recommended by the guidelines, and the decrease in HF morbidity, its prevalence remains high. It is estimated to represent 2% to 3% of the Western population, showing an association with population aging.[1] Most epidemiological data are based on population studies from the United States and western European countries, with limited data for the Polish population. According to a recent scientific report on the Polish

WHAT IS NEW?

The definition of heart failure (HF) phenotypes is rather new. Relatively little is known about the true characteristics of patients with HF in the Polish population, who can be classified into 3 categories. The present study provides a broad characterization of the relevant phenotypes of patients hospitalized for HF. Furthermore, the information retrieved from an electronic database was validated for the diagnosis of HF, which made the results more reliable as compared with studies based on the electronic registry alone. We also identified predictors of each HF subtype. To our knowledge, this is the first publication on different subtypes of HF in individuals with a confirmed diagnosis, providing detailed characteristics of hospitalized patients with HF in Poland.

population covering the period between 2013 and 2018, despite a reduction in the incidence by 43%, the prevalence of HF increased by 11.6%. Furthermore, mortality rates were also higher by 28.5%.[2] Until 2016, phenotyping of the HF population, based on the ejection fraction (EF), was not strictly defined, and 2 main types were distinguished: HF with preserved EF (HFpEF) and HF with reduced EF (HFrEF).[3] At the time, EF was used for prognostic and therapeutic purposes or inclusion criteria for trials.[4] The accepted EF thresholds differed substantially among recently reported trials or community-based studies and registries.[5] However, since 2016, the principles of HF phenotyping in relation to the EF have been established and HF has been classified as HFrEF (for EF <40%), HF with mid-range / mildly reduced EF (HFmrEF; EF 40%–49%), and HFpEF (EF ≥50%).[3] The specificity of patients with each of these HF subtypes can be defined by a different distribution of comorbidities, demographic characteristics, and potentially a different prognosis.[5-12] Most studies based on Polish patients with HF did not distinguish the subtypes of HF.[2,13-16] Notably, the therapy decision is largely dependent on the evaluation of EF; therefore, recognition of the EF-based HF phenotype becomes crucial in this regard.

The aim of this study was to evaluate and identify factors and comorbidities related to different subtypes of HF in patients hospitalized for this condition.

PATIENTS AND METHODS It was a single-center, retrospective study using data from an electronic database of patients hospitalized at the National Institute of Cardiology in Warsaw, Poland—a tertiary cardiology center. The medical records of the patients were retrieved from hospital databases based on the billing codes (Diagnosis-Related Group classification system) to the payer of medical services (National Health Fund) that refer to hospitalization due to HF.

To identify patients eligible for the analysis, we searched the entire electronic hospital database for billing codes corresponding to hospitalizations for HF, both elective and emergency, between January 2014 and May 2019. For individuals with multiple hospitalizations, we used the first event for further analysis. All individuals identified in the electronic search were verified for the diagnosis of HF by designated physicians.[3] After verification of the HF diagnosis, we excluded the patients who underwent heart transplantation / implantation of left ventricular assist devices or were misdiagnosed (40 patients) and those who had congenital heart disease (20 patients). Individuals with missing data on EF were also excluded (21 patients). Chronic HF was declared when the diagnosis was made more than 6 months prior to inclusion in the study. All information regarding the medical history, such as comorbidities or invasive procedures performed, was obtained from the medical records provided by the attending physicians. This information was supplemented with data from the National Health Fund database, the only institution providing public health insurance in Poland, which covers almost 100% of the Polish population, using diagnostic (*International Classification of Diseases, 10th Revision* [ICD--10]) and procedure (ICD-9) catalogs. The database included information from outpatient and inpatient care providers. Therefore, the medical history information included data from before hospitalization (available as of January 2014) or obtained during index hospitalization. The pharmacotherapy data were based on discharge notes. An optimal dose of angiotensin-converting enzyme inhibitors (ACEIs), β-blockers (BBs), or mineralocorticoid receptor antagonists (MRAs) was considered to be at least 50% of the dose recommended in the guidelines. The use of catecholamines was defined as the use of epinephrine, norepinephrine, dobutamine, or dopamine in high doses. Patients who underwent left ventricular assist device implantation or heart transplantation during hospitalization were censored as alive (4 patients with HFrEF).

All patients were phenotyped based on the EF assessed during an echocardiography examination. Individuals with EF below 40% were labeled as HFrEF, those with EF between 40% and 49%, as HFmrEF, and those with EF equal or greater than 50%, as HFpEF, following the recommendations in force at the time.[3] The final study population consisted of 2601 patients. The study protocol was approved by the Biomedical Ethics Committee of the National Institute of Cardiology.

Statistical analysis The distribution of quantitative data was verified by the Shapiro–Wilk test in the total sample and in the 3 HF subgroups. In all cases, the data did not follow a normal distribution, so the variables were presented as medians with interquartile ranges. The qualitative variables were presented as percentages, both in the total sample and in the subgroups divided by the subtype of HF.

Comparisons of the distribution of quantitative data among the 3 subtypes of HF were made using the Kruskal–Wallis test, while the χ^2 test

TABLE 1 Baseline characteristics of different heart failure phenotypes

Characteristic	HF total (n = 2601)	HFrEF (n = 1608)	HFmrEF (n = 331)	HFpEF (n = 662)	*P* value[a]
Male sex	70.1	81.3	68.3	44	<0.001
Age, y	63.9 (55.1–72.4)	61.6 (53.5–68.4)	66.5 (55.5–74.9)	70.5 (60.1–80.4)	<0.001
Ischemic etiology	40.1	49.8	34.4	19.3	<0.001
Chronic HF	86	87.6	82.2	83.9	0.007
Duration of hospitalization, d	7 (3–12)	8 (3–12)	5 (2–10)	7 (3–12)	<0.001
Emergency admission	45.7	40.8	45.3	57.7	<0.001
Catecholamines used during hospitalization	13.3	14.5	9.7	12.2	0.04
Death during hospitalization	4.3	4.8	3.9	3.5	0.35
Aortic stenosis	9	5.3	9.7	17.7	<0.001
Hypertension	81.4	78.2	85.2	87.3	<0.001
Ischemic heart disease	71.5	75.2	69.2	63.6	<0.001
Diabetes mellitus	37.1	38.7	36.3	33.5	0.07
Atrial fibrillation	58.4	55.6	59.5	64.5	<0.001
Stroke (any type)	12.1	12.7	10.3	11.6	0.43
Anemia	19	15.9	20.5	25.5	<0.001
Renal failure	33.9	33.6	29.3	36.9	0.06
COPD/asthma	25	24.5	20.5	28.3	0.02
Thyroid disease	29.4	27.5	27.8	34.7	0.002
Cancer	24.7	19.6	28.7	32.2	<0.001
Comorbidities, n	5 (3–6)	4.5 (3–6)	4 (3–6)	5 (3–6)	0.13
PCI	30.2	36.6	27.2	16.2	<0.001
CABG	11.8	12.9	12.7	8.8	0.02
ICD (including ICD-CRT)	42.6 (9.3)	56.5 (13.8)	23.6 (3.9)	18.3 (0.9)	<0.001
Ablation	11.2	12.4	12.1	7.6	0.003
Valvular surgery	13.5	10.9	13.9	19.6	<0.001
Mitraclip procedure	1.1	1.6	0.3	0.2	0.002

Categorical variables are presented as percentage and continuous variables as median (interquartile range).

a For difference between the subgroups

Abbreviations: CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; CRT, cardiac resynchronization therapy; HF, heart failure, HFmrEF, heart failure with mildly reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; ICD, implantable cardioverter defibrillator; PCI, percutaneous coronary intervention

was used to compare the frequency of qualitative trait categories. Logistic regression with dummy variables was used to identify the predictors of each HF subtype. Three separate analyses were performed to allow for a comparison of odds ratios (ORs) for: (1) HFrEF vs HFmrEF and HFpEF (combined, reference); (2) HFmrEF vs HFrEF and HFpEF (combined, reference); and (3) HFpEF vs HFrEF and HFmrEF (combined, reference) for the various parameters assessed in the study. Variables that were significant in the univariable analysis were included in multivariable analyses. ORs with 95% CIs were calculated. The areas under the curve were calculated to assess the accuracy of the classification in the final models.

Ordered logistic regression was used to calculate the odds of a higher EF phenotype, with the same independent variables as those used in the logistic analyses. Similarly, only factors that were significantly associated in the univariable analyses were included in multivariable models, and ORs with 95% CIs were calculated.

All data analyses were performed with Stata Statistical Software: Release 17 (StataCorp LLC, College Station, Texas, United States). The significance level was set at a *P* value lower than 0.05.

RESULTS From January 2014 to May 2019, a total of 2601 patients were enrolled in the study. These included 1608 patients (62%) with HFrEF, 331 patients with HFmrEF (13%), and 662 patients with HFpEF (25%). Most individuals with HFrEF were classified as elective admissions, whereas urgent admissions were more common among participants with HFmrEF or HFpEF. The duration of hospitalization was comparable between the groups, with the longest duration for HFrEF (TABLE 1). Survival rates at discharge were 95.2%, 96.1%, and 96.5% for HFrEF, HFmrEF, and HFpEF, respectively, and were comparable.

Patient characteristics The subset of patients with HFpEF included the oldest group of participants, and 56% of them were women. On the contrary, individuals with both HFrEF and

TABLE 2 Echocardiography and laboratory test results

Variable	HF total (n = 2601)	HFrEF (n = 1608)	HFmrEF (n = 331)	HFpEF (n = 662)	*P* value[a]
Left ventricular diastolic diameter, mm	61 (52–69)	66 (60–73)	55 (50–60)	48 (44–53)	<0.001
Ejection fraction, %	32 (22–50)	25 (20–30)	45 (40–45)	60 (54–65)	<0.001
Left atrial size, cm^2	30 (25–36.5)	31 (26–37.3)	28 (23–35)	28 (23.5–34)	<0.001
Right ventricular size, mm	37 (32–42)	38 (32–44)	35 (31–40)	34 (30–40)	<0.001
TAPSE, mm	18 (14–21)	17 (14–19)	19 (15–22)	19 (16–22)	<0.001
Right ventricular pressure, mm Hg	42 (34–55)	44(35–55)	39 (30–51)	41 (33–55)	<0.001
Significant mitral regurgitation	44.1	53	30.3	29.2	<0.001
Significant tricuspid regurgitation	35.7	37.2	27.7	36	0.005
Creatinine, mg/dl	1.1 (0.9–1.4)	1.13 (0.97–1.4)	1.1 (0.9–1.4)	1.06 (0.9–1.4)	<0.001
Urea, mg/dl	47.6 (36.1–71.7)	47.6 (36.4–70)	50.5 (37.9–79.1)	46.8 (34.6–79.1)	0.18
Sodium, mmol/l	140 (137–142)	140 (137–142)	140 (138–142)	140 (138–142)	0.002
Potassium, mmol/l	4.5 (4.2–4.86)	4.5 (4.2–4.86)	4.45 (4.15–4.74)	4.4 (4.1–4.7	<0.001
ALT, U/l	23 (16–35)	24 (17–37)	21.6 (16–31.5)	20 (15–29)	<0.001
AST, U/l	25 (19–34)	25 (20–35)	23 (19–33)	24 (19–32)	0.004
Bilirubin, mg/dl	0.8 (0.54–1.3)	0.9 (0.59–1.45)	0.65 (0.46–1.11)	0.69 (0.5–1.09)	<0.001
Hemoglobin, g/dl	13.6 (12.3–14.8)	13.9 (12.6–15)	13.4 (12–14.6)	13 (11.4–14.3)	<0.001
Leukocytes, T/ul	7.52 (6.25–9.22)	7.57 (6.34–9.23)	7.26 (6.12–8.91)	7.51 (6–9.35)	0.18
Neutrophil/lymphocyte ratio	2.97 (2.06–4.45)	2.95 (2.06–4.34)	2.79 (2.08–4.07)	3.15 (2.03–5.1)	0.06
Lymphocytes, %	22.06 (16.16–28.65)	22.6% (16.4–28.6)	22.73 (17.3–28.57)	21.2 (14.34–28.72)	0.03
Platelets, T/ul	195 (156–240)	192 (154–234)	194 (161–247)	203.5 (159–252)	<0.001
RDV-CV, %	14.7 (13.7–16.1)	14.7 (13.7–16.3)	14.2 (13.2–15.7)	14.6 (13.7–15.9)	<0.001
CRP, mg/dl	0.4 (0.17–1.28)	0.4 (0.17–1.18)	0.38 (0.14–1.2)	0.42 (0.18–1.69)	0.33
NT-proBNP, pg/ml	2201 (819.7–5237.5)	2741.5 (1071–6078)	1336 (402.7–4090)	1446 (509.8–3689)	<0.001
Uric acid, mg/dl	7.08 (5.7–8.6)	7.38 (6.03–8.9)	6.25 (5.2–7.83)	6.5 (5.3–7.82)	<0.001

Categorical variables are presented as percentage and continuous variables as median (interquartile range).

a For difference between the subgroups

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; CRP, C-reactive protein; NT-proBNP, N-terminal pro–B-type natriuretic peptide; RDW-CV, red cell distribution width–coefficient of variation; TAPSE, tricuspid annular plane systolic excursion; others, see TABLE 1

HFmrEF were younger by 9 and 4 years, respectively. The patients with HFrEF and HFmrEF were more often male. Most of the patients had a history of HF shorter than 6 months, and this was observed mainly in the HFmrEF and HFpEF subgroups. The ischemic etiology of HF was more frequent in the patients with HFrEF and was the lowest in those with HFpEF (TABLE 1).

The number of comorbidities ranged from 0 to 12 per patient, with the vast majority of patients (>97%) having at least a single comorbidity. The median number of comorbidities for all HF phenotypes was from 4 to 5. The most frequent comorbidities were hypertension (most common in HFpEF), ischemic heart disease (most prevalent in HFrEF), atrial fibrillation (most common in HFpEF), diabetes mellitus and renal dysfunction (almost equally distributed between the subtypes of HF), and pulmonary disease (most prevalent in HFpEF). Invasive cardiology procedures, such as percutaneous coronary intervention or ablation, were the most common in HFrEF, with significantly lower numbers in the remaining HF groups. On the other hand, valvular surgeries were the most frequent in HFpEF (TABLE 1).

Echocardiography and laboratory test results As presented in TABLE 2, the size of the left and right ventricles and the left atrium area were larger in HFrEF than in HFpEF or HFmrEF. Tricuspid annular plane systolic excursion was borderline in HFrEF but it was normal in HFpEF and HFmrEF. Significant mitral regurgitation was observed in 53% of patients with HFrEF, while it was less common in the remaining HF groups. On the other hand, tricuspid regurgitation was diagnosed with a similar frequency in HFrEF and HFpEF, while aortic stenosis was the most prevalent in HFpEF. The estimated right ventricular pressure was elevated in all HF phenotypes, reaching the highest values in HFrEF.

With respect to the biochemical tests, the highest levels of creatinine, transaminases, and bilirubin were observed in HFrEF. The leukocyte count and the neutrophil to lymphocyte ratio were similar in all HF subgroups, while the hemoglobin level was lowest in HFpEF. The level of N-terminal

TABLE 3 Pharmacotherapy by heart failure subtypes

Pharmacotherapy	HF total (n = 2601)	HFrEF (n = 1608)	HFmrEF (n = 331)	HFpEF (n = 662)	*P* value[a]
ACEI	86	91	87.4	73.2	<0.001
ACEI optimal dosage	58.1	62.1	62.5	46.1	<0.001
BB	96.1	97.9	94.4	92.6	<0.001
BB optimal dosage	61.6	65.7	60.9	52	<0.001
MRA	73.9	84.5	64.6	53.2	<0.001
MRA optimal dosage	68.6	79	59.7	48	<0.001
Diuretics	87.2	91.6	81	79.5	<0.001
ARNI	0.46	0.7	0	0	0.001
VKA/DOAC	59	58.7	54.9	61.8	0.11
Digoxin	15.5	17	12.3	13.5	0.03
Amiodarone	17.5	21.3	14.1	9.9	<0.001

Data are presented as percentages.

a For difference between the subgroups

Abbreviations: ACEI, angiotensin-converting enzyme inhibitors; ARNI, angiotensin receptor-neprilysin inhibitor; BB, β-blockers; DOAC, direct oral anticoagulants; MRA, mineralocorticoid receptor antagonists; VKA, vitamin K antagonists; others, see TABLE 1

pro–B-type natriuretic peptide was the highest in HFrEF (TABLE 2).

Pharmacotherapy The pharmacotherapy pattern is presented in TABLE 3. In HFrEF, ACEIs, BBs, and diuretics were used in more than 90% of the participants, while the prevalence of MRA use reached almost 85%, and ARNIs were recommended in a negligible percentage of patients. Furthermore, in HFrEF, optimal doses of ACEIs, BBs, and MRAs were recommended in approximately two-thirds of patients. In the remaining HF subgroups, all these drugs, including diuretics, were used in a much smaller proportion of patients (TABLE 3).

Predictors of heart failure phenotypes Of the selected potential predictors of HFrEF vs HFmrEF and HFpEF (combined), the variables that were significantly associated with a lower likelihood of this HF phenotype by univariable logistic regression were older age, female sex, aortic stenosis, hypertension, anemia, any thyroid conditions, atrial fibrillation, and malignancy. On the contrary, a longer history of HF, ischemic etiology, coronary artery disease, diabetes mellitus, and liver failure significantly increased the odds of HFrEF. Almost all of the variables remained significant in the multivariable model, with the exception of atrial fibrillation and thyroid abnormalities (FIGURE 1A).

Opposite results were observed in the model predicting HFpEF vs HFrEF and HFmrEF (combined), with the exception of chronic history of HF, which was not significant. In the multivariable analysis, atrial fibrillation, anemia, and thyroid disorders were insignificant (FIGURE 1B).

The model predicting HFmrEF vs HFrEF and HFpEF (combined) revealed a much smaller number of significantly associated predictive variables, limited only to ischemic etiology, longer history of HF, and chronic obstructive pulmonary disease / asthma, all showing a negative association. However, in the multivariable analysis, only ischemic etiology remained significant (FIGURE 1C).

The findings from the multivariable ordered regression model were generally in line with those from the logistic regression analysis, showing that female sex (OR, 3.06; *P* <0.001), aortic stenosis (OR, 2.18; *P* <0.001), hypertension (OR, 1.64; *P* <0.001), cancer (OR, 1.45; *P* <0.001), anemia (OR, 1.3; *P* = 0.02), and age (OR, 1.04; *P* <0.001) increased the probability of HFpEF as compared with the reference (HFmrEF and HFrEF), while chronic HF (OR, 0.68; *P* = 0.002), coronary artery disease (OR, 0.72; *P* = 0.004), ischemic etiology (OR, 0.33; *P* <0.001), diabetes mellitus (OR, 0.82; *P* = 0.033), renal failure (OR, 0.77; *P* = 0.011), and liver failure (OR, 0.55; *P* = 0.007) decreased it. Similar conclusions could be drawn for the comparison of HFmrEF and HFpEF (combined) vs HFrEF (reference).

DISCUSSION

The results of the present study provide detailed characteristics of hospitalized patients with HF. To our knowledge, this paper is the first to describe different subtypes of HF in a large population of HF patients from Poland. A very important finding of this study was that patients stratified by different HF phenotypes differed in terms of demographic and clinical characteristics, including comorbid disease burden, and therapeutic strategies. Of note, the picture of HF varies between countries, which justifies conducting the study in different populations.

In our research, as in many other studies, the majority of the HF population comprised individuals with HFrEF.[5,7,17,18] It should be noted that the proportion of patients with HFpEF was relatively smaller than in some of the previous

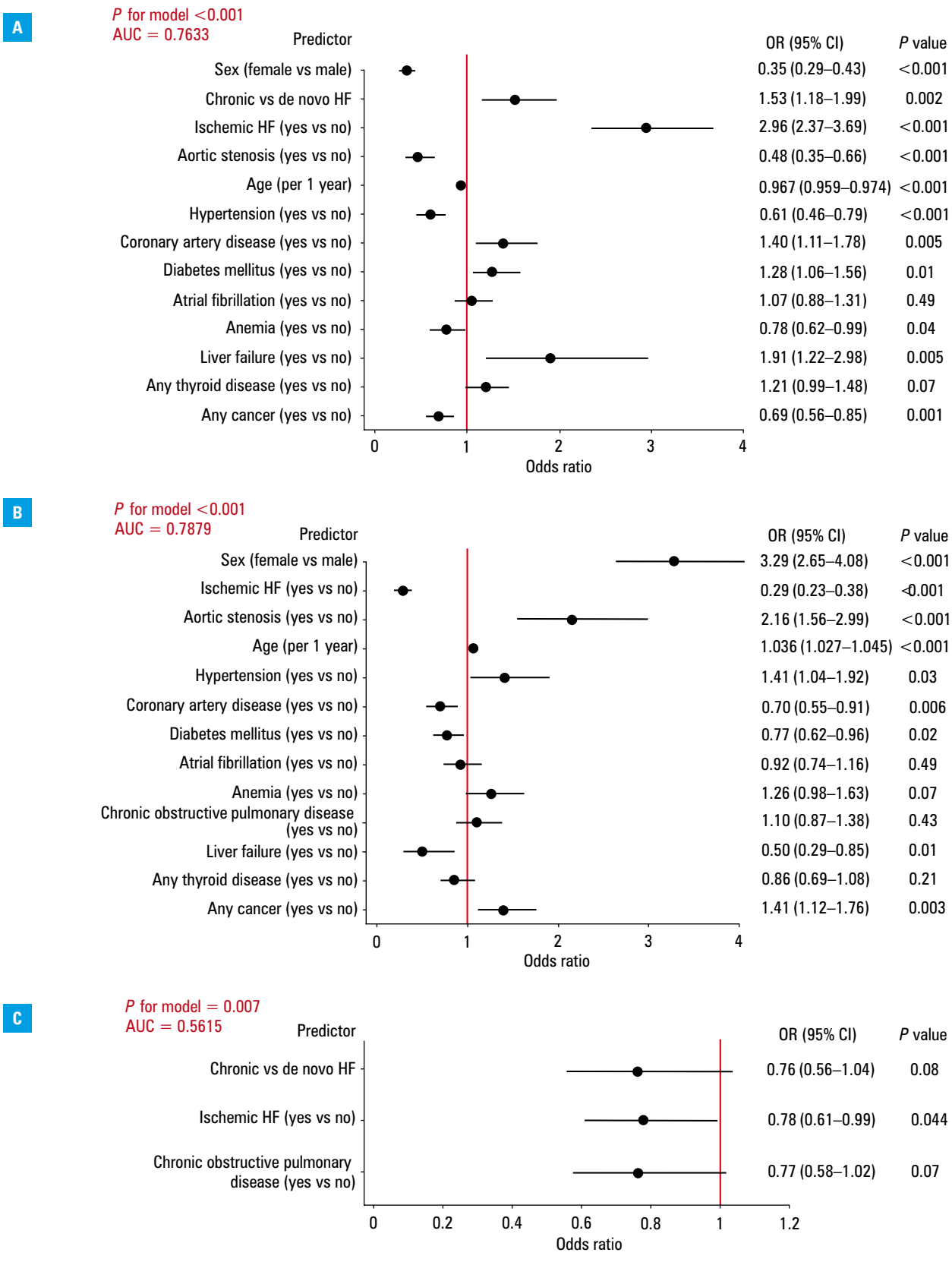

FIGURE 1 Predictors of heart failure phenotypes in multivariable logistic regression analysis; **A** – HFrEF vs reference (HFmrEF and HFpEF); **B** – HFpEF vs reference (HFrEF and HFmrEF); **C** – HFmrEF vs reference (HFrEF and HFpEF)
Abbreviations: AUC, area under the curve; others, see **TABLE 1**

reports.[9,10,19] However, data from ambulatory registries reported an even smaller number.[18] Furthermore, HFmrEF constituted only a small proportion of the total HF sample, which is consistent with other studies performed in hospital settings.[19,20] In general, in ambulatory settings, the prevalence of HFmrEF is higher.[7,18] Interestingly, the analysis of the proportions of emergency hospitalizations showed that it was highest in HFpEF. Similar findings were also reported in studies on advanced HF[11]; however, contrary results were noted in the elderly patients with acute

HF.[12] The observed discrepancies may have been due to the specificity of patients treated at the tertiary cardiac center. The high proportion of individuals with HFpEF qualified for emergency admission may be due to a significant selection bias regarding patients referred to this center.

According to previous publications, patients with HFrEF tended to be younger and more frequently male than those with HFpEF and HFmrEF, while the opposite was true for HFpEF. This pattern was observed regardless of the clinical setting in which the study was performed.[5,7,9-11,19,21] It should also be underlined that the Polish HF population is generally younger than populations analyzed in studies from other countries.[14,22]

In general, the number of comorbidities per patient was the same in all subgroups but higher than in other studies.[10,14,15] However, there were significant differences in the distribution of comorbidities between the subgroups. Compared with the remaining subtypes, HFpEF had the highest prevalence of hypertension, atrial fibrillation, anemia, renal failure, thyroid dysfunction, chronic obstructive pulmonary disease, and cancer. In HFrEF, ischemic heart disease and diabetes were the most common comorbidities. The highest frequency of comorbidities reported in HFpEF, mainly noncardiovascular, was consistent with the advanced age and an increased risk of health problems typical of patients with this HF subtype.[5] A surprisingly high percentage of cancer cases was found in our population as compared with previous studies.[7,23] This may be due to the specificity of our center, where the most complex patients are referred to and treated.

The etiology of the HF subtypes analyzed was consistent with that reported in previous publications, showing that ischemic etiology was most common in HFrEF, while nonischemic etiology was most common in HFpEF. On the contrary, the frequency of ischemic etiology in HFmrEF is somewhere between the values for HFrEF and HFpEF.[5,7,18] This may be due to the composition of the HFmrEF subpopulation, which may include patients with a primary diagnosis of HFmrEF or a mix of individuals who improved from HFrEF or experienced worsening of HFpEF.[24]

The history of revascularization was consistent with the history of ischemic heart disease in all the HF subgroups, showing the highest incidence of percutaneous coronary intervention or bypass surgery in HFrEF, followed by HFmrEF.[10,16,17] Despite the relatively high prevalence of ischemic heart disease in HFpEF, as compared with HFrEF, the proportion of revascularization was almost 50% lower in this group. This discrepancy was not observed in some previous reports[10,17] but it was described in the manuscript based on the European Society of Cardiology Heart Failure Long-Term (ESC-HF-LT) registry.[5] In a previous publication analyzing Polish data from the ESC-HF-LT registry, the percentage of revascularized patients was 35%; however, there was no information on the HF phenotypes.[16] In our study, the rate of valvular surgeries, most frequently reported in HFpEF, resembled data from the ESC-HF-LT registry.[5] It could be related to advanced age of the patients with this HF subtype.

There is a great variability with respect to the frequency of implantable cardioverter defibrillator (ICD) implantations, depending on the population studied. In our study, a relatively high percentage of patients with ICD in the HFpEF or HFmrEF subgroup was highly suggestive of the benefits of the applied strategies that led to dynamic changes in EF, confirming that both groups could include individuals who had improved from HFrEF.[24] In our population of patients with HF, recruited mainly from a single region of Poland, the rate of ICD implantations exceeding 50% was rather high in comparison with the rates reported in other countries. Data from the ESC-HF-LT registry showed a rate of 35%,[5] in Italy it was 28%,[7] while in Japan it was even smaller, reaching 15%.[9] A previous publication on the Polish population also showed much smaller numbers.[16] This can be explained in part by differences in the recruitment period in the cited studies and perhaps also by differences in the reimbursement policy.

With respect to echocardiography, the most pronounced differences among the groups were in the left ventricular size and EF, as indicated by the categorization of HF subtypes. Remodeling of the right and left ventricles and the left atrium was the most pronounced in HFrEF, and it was accompanied by elevated right ventricular pressure. However, it is important to note that except for the previously mentioned left ventricular diameter, the echocardiographic parameters for particular HF subtypes were not very different from one another. This is in line with the long history of HF reported by most patients, which could cause the development of pathophysiological changes, including electrical remodeling.[5]

In the previous ESC guidelines,[3] ACEIs, BBs, MRAs, and ARNIs were recommended as life-saving medications in HFrEF. There were no such recommendations for HFmrEF or HFpEF. In comparison with other publications, the percentage of patients who used the recommended pharmacotherapy was relatively high in our study, except for MRAs, the use of which was consistent with reports from European countries[5,7,17,18] and also with previous Polish data.[14,16,22] Furthermore, the HF phenotype did not drastically influence the pharmacotherapy pattern.[5,7] This tendency could be caused by the comorbidity profiles in the HF subtypes that determined the pharmacotherapy, but may also be the result of the continuation of treatment in patients with previously reduced EF.[5,16] On the other hand, in recent guidelines on HF management[25] all the drugs mentioned above were proposed for HFmrEF, and in recent FDA statements, MRA was also accepted for the treatment of HFpEF.[24]

Based on the results of biochemical tests, which reflect organ functioning, it can be speculated that

any abnormalities were due to decreased cardiac output and congestion, as patients with HFrEF had both right and left ventricular involvement. On the other hand, the hemoglobin level was the lowest in HFpEF, which is in line with the results of previous publications.[7,9,11] The leukocyte count, which is a risk factor for a poor prognosis,[26] was comparable in patients with all the subtypes of HF, as in other reports.[9,12] The level of N-terminal pro–B-type natriuretic peptide is modified by the clinical status of the patient. Therefore, the values reported in the current study differed between ambulatory and hospitalized patients with advanced HF.[7,11,18] The lowest values in the patients with HFmrEF were also documented in the ESC-HF-LT registry, supporting the idea that a significant number of these patients were in the improvement phase and a better clinical condition.[4,5]

In several previous studies, the rate of cardiovascular events during long-term observation was higher in patients with HFrEF than in other HF subtypes,[4] while some reported a similar prognosis.[24] In our population, a short-term follow-up of hospital mortality showed that the survival status at discharge was comparable for all subtypes of HF. A similar observation on the short-term prognosis was also reported in some publications,[9,11] while in others, HFrEF was associated with the worst prognosis.[5,18,19]

HFmrEF was suggested to be a milder form of HFrEF, characterized by features that resemble the latter HF phenotype.[4] Based on European data, it can be observed that patients with HFmrEF and HFrEF share many characteristics, such as predominantly male sex, younger age, ischemic etiology, and lower frequency of atrial fibrillation.[4,5] In other studies, the participants with HFmrEF were more similar to those with HFpEF in terms of some clinical features, confirming the inconsistency of different analyses.[24,27] However, it should be noted, as shown in a study by Savarese et al,[20] that the distribution of patients with EF who remain stable over time differs according to the subtypes of HF. In HFrEF and HFpEF, most of the patients (61%–75%) had the same EF at the end of the observation, while in HFmrEF, this rate was only 38%, and almost two-thirds of the patients had improved from HFrEF or had deteriorated from HFpEF.[20] It indirectly shows that HFmrEF is not a uniform category and its characteristics are mainly determined by the dominance of a particular subgroup.[4]

There are several limitations to this study that should be addressed. First, the study had a retrospective design based on coding of hospitalizations for HF for administrative purposes. Therefore, some patients with HF who were never registered as hospitalized for HF were not included. Furthermore, we analyzed only the patients from a single tertiary cardiology center in Poland, so we cannot exclude a population selection bias. In addition, some of the information on the classic factors of cardiovascular risk was not available in the medical records, which resulted in their exclusion from the analysis. Unfortunately, we did not have information on the EF trends before the study; therefore, we were unable to determine the history of possible phenotypic changes before hospitalization. Since EF evaluation was derived from the medical records, standardization was not possible, which could lead to possible differences between operators and, thus, to a possible erroneous classification of some patients. Finally, we were unable to assess the clinical status on admission or obtain information on pharmacotherapy prior to the study.

In conclusion, this was a broad description of Polish patients hospitalized due to HF, originating mainly from a single province and classified by HF subtypes, with the identification of factors strongly associated with each phenotype. HF stratified by different categories based on the EF represented different phenotypes in terms of demographics, etiology, myocardial remodeling, and organ function. HFrEF and HFpEF stood on opposite sides in most analyses. HFmrEF was unlikely to be a completely separate, standalone category, but rather a mixture of patients who had previously had HFrEF or HFpEF. It should be noted that the characteristics of the HF subtypes presented here differed in many ways from those described in studies from other countries.

ARTICLE INFORMATION

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