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Clinical pathways of patients with heart failure with preserved ejection fraction hospitalized for acute heart failure: Insights from the National Multi-Centre HF-POL Registry

Short title: Clinical pathways of HFpEF patients with HFH in HF-POL Registry

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INTRODUCTION

Heart failure with preserved ejection fraction (HFpEF) accounts for approximately half of heart failure (HF) cases worldwide [1, 2]. In recent years, significant efforts have been made to draw attention to patients with HFpEF, as these patients face a risk of death comparable to those with heart failure with reduced ejection fraction [1, 2]. Furthermore, the causes of death in HFpEF patients often extend beyond cardiology, reflecting the multimorbidity prevalent among this population [3]. Understanding the clinical journey and care schemes for HFpEF patients could significantly contribute to optimizing healthcare organization and improving prognoses. Our study aimed to describe the real-life care pathways for patients before and during hospitalization due to acute HF in the Polish HFpEF population, comparing those with and without previous HF hospitalization.

METHODS

Data source

The data was provided by the Heart Failure Poland (HF-POL) study, a multicenter observational study including patients with HF and left ventricular ejection fraction $>40\%$, conducted by the Heart Failure Association of the Polish Cardiac Society in cooperation with the Committee for Clinical Initiatives of the Executive Board as part of the Scientific Platform initiative. The HF-POL study included patients who had recognized HF (according to the 2021 European Society of Cardiology guidelines) with documented ventricular ejection fraction $>40\%$ and were either treated for HF on ambulatory basis or hospitalized for HF (HF exacerbation or HF *de novo*) with administration of intravenous therapy (diuretics and/or catecholamines and/or nitrates) [4]. The rationale and design of the HF-POL registry and baseline characteristics of all patients enrolled in the database were previously described [5, 6]. Our study includes patients with HFpEF (EF $\geq 50\%$) who were hospitalized according to the inclusion criteria of the HF-POL

study. The study has been registered in the ClinicalTrials.gov database with identifier NCT06030661.

Study group

The study included all patients with HFpEF hospitalized due to acute (de novo or decompensated) HF requiring administration of intravenous therapy and reported to the HF-POL Registry. Patients were divided into two groups: without (n = 444) and with (n = 91) previous hospitalization due to heart failure (HFH).

Statistical analysis

The normality of the variables was verified using the Shapiro–Wilk normality test. None of the continuous variables had normal distribution; thus, they were described with the median and interquartile range. The number of observations and the corresponding percentage (%) were given for categorical variables. The non-parametric Mann–Whitney U test was used to compare two independent groups. Pearson’s χ^2 test of independence (with Yates correction where necessary) was used to compare groups for qualitative variables. Results with $P < 0.05$ were considered significant. The STATISTICA PL v. 13.3 and PQStat 1.8.6 packages were used for calculations.

RESULTS AND DISCUSSION

The study included 535 patients with HFpEF hospitalized due to acute HF, of which 91 (17.0%) had at least one HFH in the last 12 months. The median age of patients was 76 (69–84) and 76 (72–84) for patients without and with at least one previous HFH, respectively. The median of EF was 55 (52–60) in both groups and N-terminal pro-B-type natriuretic peptide levels 2072 (896–4791) and 2542 (1125–5394) pg/ml, respectively. More than half of the patients (51.7%) with previous HFH had at least three hospitalizations due to HF in the last 12 months. The baseline characteristics are presented in [Table 1](#).

Patients in both groups were similar in age, sex, body mass index, heart rate, systolic and diastolic blood pressure, and N-terminal pro-B-type natriuretic peptide concentrations. There were no differences in the clinical presentation at hospital admission. The main difference in medical history was the etiology of heart failure, with a significantly higher percentage of ischemic HF in patients with prior HFH. This was associated with a more frequent history of myocardial infarction, percutaneous coronary intervention, and coronary artery bypass grafting

in this group. Patients without previous HFH more often had non-cardiovascular comorbidities (Table 1).

Patients with HFpEF and a history of at least one previous HFH were twice as likely to have a visit to the outpatient clinics before admission. Moreover, they were almost exclusively hospitalized in cardiology departments, while individuals without prior HFH were equally distributed between internal medicine and cardiology departments. Most patients without previous HFH were transferred to the hospital by emergency services — hospital emergency department and ambulance service. Individuals with previous HFH were mainly referred by general practitioners (GPs) and outpatient clinics (Table 1).

Our study, which analyzes the clinical pathways of HFpEF patients in the Polish healthcare system, shows some important facts. Firstly, most patients with the first HFH are referred to the hospital by emergency services. This suggests an insufficient awareness of heart failure among patients and GPs. Most patients admitted for the first time with acute HF presented symptoms that had been developing over a long period. In case of the appropriate awareness of HF signs and symptoms, patients should consult a primary care physician in advance to avoid exacerbation of the disease, resulting in the need for hospitalization. The primary intervention during hospitalization was intravenous diuretic therapy. Both GPs and educated, cooperating patients (self-management of HF) should be encouraged to intensify the oral diuretics therapy in the initial phase of HF exacerbation to avoid urgent HFH. Secondly, almost all patients with subsequent hospitalizations due to heart failure were admitted to the cardiology department. To efficiently distribute healthcare resources, patients should be triaged for the appropriate department specialization depending on the clinical advancement of the disease. Not all patients with exacerbation of HF require hospitalization in cardiology departments. However, our results may be biased because the HF-POL registry gathered data from selected hospitals in Poland, most of which were cardiology centers. Nevertheless, there is a need to create mechanisms to treat patients with mild HF in regional centers and to refer patients with more severe HF to high-reference centers. Lastly, the frequency of sodium-glucose co-transporter 2 use may be lower than expected because patients were enrolled before the last focus update of European Society of Cardiology guidelines. Therefore, patients had sodium-glucose co-transporter 2 administered for diabetes mellitus-related indications and not HF. Some of the problems mentioned above were described in detail in the expert opinion of the Heart Failure Association of the Polish Cardiac Society [7].

To conclude, the analysis of data on the clinical journey of HFpEF patients from the HF-POL registry hospitalized due to acute HF showed significant differences in the

management of hospital treatment between patients with and without previous hospitalization due to acute HF. Some of those observed elements require further analysis and optimization.

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Table 1. Baseline characteristics and clinical pathways of patients with heart failure with preserved ejection fraction with and without previous heart failure hospitalization (HFH)

	Without previous HFH n = 444	With at least one previous HFH n = 91	<i>P</i> -value
Age, median (IQR), years	76 (69–84)	76 (72–84)	0.28
Females, n (%)	194 (43.7)	35 (38.5)	0.36
BMI, median (IQR), mm Hg	29 (25–33)	29 (26–32)	0.87
SBP, median (IQR), mm Hg	130 (115–145)	130 (120–145)	0.65
DBP, median (IQR), mm Hg	76 (70–83)	73 (66–83)	0.63
HR, median (IQR), bpm	77 (70–90)	79 (64–95)	0.75
Ischemic etiology, n (%)	109 (24.6)	38 (41.8)	<0.001
NYHA at admission, n (%)			
NYHA I	19 (4.3)	3 (3.3)	<0.001
NYHA II	98 (22.1)	20 (22.0)	
NYHA III	156 (35.1)	53 (58.2)	
NYHA IV	113 (25.5)	15 (16.5)	
No data	58 (13.1)	0	
EF, median (IQR), %	55 (50–58)	55 (52–60)	0.008
NT-proBNP, median (IQR), pg/ml	2072 (896–4791)	2542 (1125–5394)	0.27

GFR, median (IQR), ml/kg/1.73 m ²	55 (40–61)	52 (41–67)	0.78
Length of hospital stay, median (IQR), days			
Past medical history			
Prior heart failure, n (%)	279 (62.8)	91 (100)	<0.001
No. of previous HFH			
1	0	23 (25.3)	–
2	0	21 (23.1)	
≥3	0	47 (51.7)	
Hypertension, n (%)	362 (81.5)	78 (85.7)	0.34
Hyperlipidemia, n (%)	198 (44.6)	65 (71.4)	<0.001
Diabetes mellitus, n (%)	162 (36.5)	38 (41.8)	0.34
Obesity, n (%)	147 (33.2)	37 (40.7)	0.17
Chronic kidney disease, n (%)	96 (21.6)	33 (36.3)	0.027
Atrial fibrillation, n (%)	210 (47.30)	68 (74.7)	<0.001
Myocardial infarction, n (%)	58 (12.9)	24 (25.3)	0.001
Stroke, n (%)	40 (9.0)	8 (8.8)	0.95
Peripheral arterial disease, n (%)	26 (5.9)	9 (9.9)	0.16
Smoking, n (%)			
Current	43 (9.7)	6 (6.6)	0.035
Former	159 (35.8)	22 (24.2)	
Never	242 (54.5)	63 (69.2)	
COPD, n (%)	81 (18.2)	8 (8.8)	0.027
History of SARS-CoV-2, n (%)	65 (14.6)	17 (18.7)	0.33
Procedures before admission			
History of PCI, n (%)	81 (18.2)	29 (31.9)	0.003
History of CABG, n (%)	24 (5.4)	11 (12.1)	0.019
History of cardiac ablation, n (%)	15 (3.4)	4 (4.4)	0.78

Implanted pacemaker, n (%)	71 (16.0)	17 (18.7)	0.53
Implanted ICD/CRT-P/CRT-D, n (%)	9 (2.0)	0	-
Clinical presentation of HF at hospital admission			
Peripheral oedema, n (%)	248 (55.9)	54 (59.3)	0.54
Pulmonary congestion, n (%)	158 (35.6)	42 (46.2)	0.06
Pleural effusion, n (%)	96 (21.6)	27 (29.7)	0.1
Hepatomegaly, n (%)	48 (10.8)	13 (14.3)	0.34
Jugular vein distention, n (%)	33 (7.4)	6 (6.6)	0.78
Clinical profile (the Forrester classification), n (%)			
Warm-dry	80 (18.0)	37 (40.7)	<0.001
Warm-wet	321 (72.3)	52 (57.1)	
Cold-dry	9 (2.0)	2 (2.2)	
Cold-wet	34 (7.7)	0	
Medications during hospitalization			
	Without previous HFH n = 444	With at least 1 previous HFH n = 91	<i>P</i>
Inotropes, n (%)	59 (13.3)	5 (5.5)	0.037
Intravenous diuretics, n (%)	409 (92.1)	62 (68.1)	<0.001
Intravenous nitrates, n (%)	178 (40.1)	30 (33.0)	0.2
ACEi, n (%)	237 (53.4)	48 (52.8)	0.91
ARB, n (%)	59 (13.3)	22 (24.2)	0.008
Beta-blockers, n (%)	355 (80.0)	84 (92.3)	0.005
MRA, n (%)	217 (48.9)	40 (44.0)	0.39
SGLT-2i, n (%)	46 (10.4)	23 (25.3)	<0.001

Outpatient clinic visits before admission			
Cardiologist, n (%)	150 (33.8)	81 (89.0)	<0.001
Internal medicine, n (%)	126 (28.4)	55 (60.4)	<0.001
Diabetologist, n (%)	37 (8.3)	21 (23.1)	<0.001
Pneumologist, n (%)	22 (5.0)	10 (11.0)	0.027
Nephrologist, n (%)	16 (3.6)	9 (9.9)	0.01
Department of hospitalization			
Internal medicine, n (%)	226 (50.9)	1 (1.1)	<0.001
Cardiology, n (%)	216 (48.7)	90 (98.9)	
ER with no data on admission, n (%)	2 (0.4)	0	
Where patients were referred from			
General practitioner, n (%)	108 (24.5)	27 (29.7)	<0.001
Ambulance service, n (%)	146 (33.1)	7 (7.7)	
Emergency department, n (%)	139 (31.5)	34 (37.4)	
Outpatient clinic, n (%)	48 (10.9)	23 (25.3)	
Where patients were discharged to			
Home, n (%)	189 (42.6)	72 (79.2)	<0.001
Another hospital, n (%)	14 (3.1)	5 (5.5)	
Social welfare home, n (%)	2 (0.5)	1 (1.1)	
No data, n (%)	239 (53.8)	13 (14.3)	

Abbreviations: ACEi, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; BMI, body mass index; CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; CRT-D, cardiac resynchronization therapy defibrillator; CRT-P, cardiac resynchronization therapy pacemaker; DBP, diastolic blood pressure; EF, ejection fraction; GFR, glomerular filtration rate; HF, heart failure; HFH, heart failure hospitalization; HR, heart rate; ICD, implantable cardioverter-defibrillator; IQR, interquartile range; MRA, mineralocorticoid receptor blocker; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; SARS-CoV-2, severe acute respiratory syndrome Coronavirus 2; SBP, systolic blood pressure; SGLT2i, sodium-glucose co-transporter 2 inhibitors