ORIGINAL ARTICLE

Two-year prognosis of patients hospitalized for decompensated heart failure in a district general hospital

Małgorzata Dobrowolska[1], Paweł Miękus[1], Michał Świątczak[2], Grzegorz Raczak[2], Ludmiła Daniłowicz-Szymanowicz[2]

1 Department of Cardiology, Saint Vincent de Paul Hospital, Gdynia, Poland
2 Department of Cardiology and Electrotherapy, Medical University of Gdańsk, Gdańsk, Poland

KEY WORDS
exacerbation, heart failure, rehospitalization, risk factors

ABSTRACT

BACKGROUND Patients hospitalized for heart failure (HF) exacerbation tend to have a poor prognosis. Most previous studies were performed in large clinical centers and detailed analyses of patients with HF hospitalized in district general hospitals are lacking.

AIMS The aim of this study was to assess the outcomes of patients admitted with HF exacerbation to a district general hospital.

METHODS We retrospectively enrolled patients hospitalized for HF exacerbation in the years 2010 to 2011 (191 patients) and 2016 to 2017 (203 patients). The primary and secondary endpoints were all-cause mortality and rehospitalization due to HF exacerbation, respectively, within a 2-year follow-up.

RESULTS Compared with patients hospitalized from 2010 to 2011, those hospitalized from 2016 to 2017 had more favorable clinical parameters and more appropriate pharmacological treatment; however, the rate of implantable cardioverter-defibrillator and resynchronization device use remained low. The overall mortality decreased from 44% between 2010 and 2011 to 33% between 2016 and 2017 (P = 0.03), but the number of rehospitalizations increased from 26% to 41%, respectively (P <0.001). Male sex, low systolic blood pressure, symptoms of right HF, and renal dysfunction were independent risk factors for the primary endpoint. Symptoms of right HF, renal dysfunction, left ventricular ejection fraction below 24%, and low systolic blood pressure independently predicted the secondary endpoint.

CONCLUSIONS The prognosis of patients hospitalized for decompensated HF in a regional district hospital was poor. Despite some improvement in pharmacological treatment, which probably led to reduced all-cause mortality, there was a low rate of implantable electronic device use and a high rate of rehospitalizations due to HF exacerbation, which needs further elucidation.

Correspondence to:
Ludmiła Daniłowicz-Szymanowicz, MD, PhD, Department of Cardiology and Electrotherapy, Medical University of Gdańsk, ul. Dębinki 7, 80-952 Gdańsk, Poland, phone: +48 58 349 39 10, email: ludwik@gumed.edu.pl
Received: November 24, 2020.
Revision accepted: January 18, 2021.
Published online: January 19, 2021.
Kardiol Pol. 2021; 79 (3): 302-310
doi:10.33963/KP.15763

INTRODUCTION Heart failure (HF) is a significant clinical problem that is estimated to affect over 37 million people worldwide,[1] including more than 8 million adults in the United States.[2] In Poland, HF affects about one million people, and additional 250 000 cases are projected over the next 25 years.[3] It is predicted that over the next decade, the prevalence of HF will surpass that of all other cardiovascular diseases[4] and will increase by 46% from 2012 to 2030.[5] This is due to a number of reasons, including an increase in the prevalence of HF with population aging, as well as a predicted increase in the incidence of concomitant diseases such as diabetes and hypertension.[6] Despite significant advances in pharmacological and device-based treatments, the mortality rate of HF remains high.[4,7,8]

Hospitalization due to HF decompensation is the leading cause of hospital admissions, particularly in patients over 65 years of age,[9] and has profound consequences including poor prognosis and remarkable healthcare expenses.[10] According to data from the Organization for

WHAT'S NEW?

This single-center, retrospective study assessed the 2-year prognosis of patients hospitalized for decompensated heart failure (HF) in 2 time periods: 2010–2011 and 2016–2017. The main advantage of this study is that the included patients were hospitalized in a district general hospital, rather than a large clinical center, where the prognosis of patients hospitalized due to HF decompensation is poor. Our study proved better clinical characteristics and lower all-cause mortality of patients hospitalized in the years 2016 to 2017 compared with those hospitalized between 2010 and 2011. However, the inefficient use of electrotherapy and still high rate of rehospitalizations due to HF exacerbation emphasize the need for taking appropriate measures to improve the situation.

Economic Co-operation and Development, Poland has the highest rate of hospitalization due to HF exacerbation.[11] Hospitalization due to HF exacerbation is a significant predictor of further deterioration and is associated with an almost 50% risk of rehospitalization within the next 6 months and a 1-year mortality rate as high as 30%.[12] Therefore, identifying patients at the highest risk of rehospitalization and death is of key importance to improve clinical outcomes. Most previous studies were based on patients hospitalized in large clinical centers[13-15] and there are limited data from regional district hospitals[16,17]; notably, to our knowledge, there have been no data collected in Poland. Given the known differences in characteristics between patients admitted to district general hospitals and those recruited into large clinical trials, a detailed analysis of patients with HF hospitalized in regional district hospitals is essential to improve our knowledge of the optimal treatment of that population. Therefore, we aimed to assess the prognosis of patients hospitalized for HF exacerbation in a regional district hospital.

METHODS The study was a retrospective analysis of all patients hospitalized in the cardiology department of Saint Vincent de Paul Hospital in Gdynia, Poland, with a diagnosis of acutely decompensated chronic HF and new-onset acute HF[18] within 2 periods of time: 2010 to 2011 and 2016 to 2017. The data were obtained by reviewing hospital medical records, electronic patient records from the Polish National Health Fund (Polish, Narodowy Fundusz Zdrowia), and the local death registry of Gdynia. Exclusion criteria were as follows: age below 18 years, New York Heart Association (NYHA) functional class I or II on hospital admission, and no information regarding clinical signs of HF. Patient records were also reviewed to obtain information on biometric parameters, medical history (with a particular emphasis on comorbidities, coronary artery status, and implanted devices), previous treatments, physical examination findings documented during hospitalization, and laboratory, electrocardiographic, and echocardiographic data. All patients were followed up for 2 years. All of the abovementioned clinical data were compared between patients hospitalized in the years 2010 to 2011 and 2016 to 2017. The primary endpoint was all-cause mortality, and the secondary endpoint, rehospitalization due to HF exacerbation. The analysis also included in-hospital mortality. The Local Ethics Committee of Medical University of Gdańsk approved the study protocol (NKBBN/619/2018). This was a retrospective study of data routinely collected in clinical practice; therefore, the requirement for written and informed consent was waived.

Statistical analysis Continuous data were presented as median and interquartile range, and categorical variables, as numbers and percentages. The Shapiro–Wilk test was performed to determine whether data were normally distributed. Comparisons between patients hospitalized from 2010 to 2011 and 2016 to 2017 were assessed with the Mann–Whitney test or Fisher exact test for variables that followed distribution other than normal. The predictive ability of the identified variables was tested with receiver operating characteristics (ROC) analysis, producing areas under the curve, and adequate cutoff values were identified according to the best coupling of sensitivity and specificity values. The association between the analyzed parameters and the endpoints was assessed using Cox hazard models. Multivariable analysis (multiple Cox proportional hazards regression model) was applied to continuous data (dichotomized according to the cutoff values identified in ROC analyses) and categorical data associated with each endpoint separately (P value of 0.05 or less); the set of variables accepted for the model was determined by the backward elimination method from the set of all statistically significant predictors. All results were considered significant at a P value less than 0.05. Statistical analysis was conducted using the Statistica software, version 12.0 (StatSoft, Tulsa, Oklahoma, United States) and R software, version 3.1.2 (R Core Team, Vienna, Austria).

RESULTS We retrospectively enrolled 191 patients hospitalized for HF exacerbation in the years 2010 to 2011 and 203 patients in 2016 to 2017 (90 patients were hospitalized in 2016, including 32 hospitalized before August 2016 when the European Society of Cardiology (ESC) guidelines on the treatment of HF[6] were published; 2 patients hospitalized in the years 2010 to 2011 were enrolled in the time period from 2016 to 2017).

Clinical characteristics The age of patients in both study groups was similar: median (interquartile range), 73 (63–81) years in patients

hospitalized between 2010 and 2011 and 70 (63–80) years in those hospitalized between 2016 and 2017; most older patients were male. More than half of the patients were diagnosed with coronary artery disease. As compared with patients hospitalized between 2016 and 2017, those hospitalized in the years 2010 to 2011 had a higher rate of myocardial infarction, diabetes, hypertension, atrial fibrillation / flutter, dementia, and NYHA functional class IV during hospitalization. Those patients also had a significantly higher heart rate on admission. The distribution of the underlying causes of hospitalization due to HF exacerbation was similar for both study groups, except acute coronary syndromes, which were a less frequent cause in the years 2016 to 2017. In approximately one-third of patients, the direct cause of HF exacerbation was unknown. Detailed data are presented in TABLE 1.

Laboratory and echocardiographic parameters Compared with patients hospitalized between 2016 and 2017, those hospitalized in the years 2010 and 2011 had significantly lower sodium levels and glomerular filtration rate yet higher C-reactive protein, glucose, high-sensitivity troponin T, and low-density lipoprotein cholesterol levels. The level of N-terminal fragment of the prohormone brain natriuretic peptide was not routinely measured in patients hospitalized in the years 2010 to 2011, making it impossible to compare this parameter between the study groups. Left ventricular ejection fraction (LVEF) and the percentage of patients with LVEF lower than or equal to 40% (which is diagnostic of HF with reduced LVEF according to the current guidelines)[6] did not differ between the groups. Patients hospitalized in the years 2016 to 2017 had more features of significant diastolic dysfunction, larger left atria, and higher right ventricular systolic pressure (TABLE 1).

Pharmacological treatment The pharmacological management of patients in both study groups was in line with the current guidelines at that time. Between 2016 and 2017, most patients received angiotensin-converting enzyme inhibitors or sartans and β-blockers at discharge. There was a reduction in the frequency of spironolactone use (from 49% to 26%) in favor of eplerenone (from 4% to 24%), a significant reduction in the use of antiplatelet drugs (46% to 30%) in favor of anticoagulants (51% to 68%), and a reduction in the use of vitamin K antagonists (VKAs) and low-molecular-weight heparin (from 51% to 32%) in favor of non–vitamin K antagonist oral

TABLE 1 Baseline clinical characteristics of the study groups (continued on the next page)

Parameter	2010–2011 (n = 191)	2016–2017 (n = 203)	*P* value
Male sex	116 (61)	144 (71)	0.03
Age, y	73 (63–81)	70 (63–80)	0.08
Medical history			
Coronary artery disease	125 (67)	126 (63)	0.52
Previous myocardial infarction	97 (52)	81 (41)	0.03
Revascularization (PCI / CABG)	110 (58)	97 (48)	0.06
Malignant ventricular arrhythmias	21 (11)	21 (10)	0.83
Atrial fibrillation / flutter	106 (56)	68 (34)	<0.001
Hypertension	135 (71)	75 (37)	<0.001
Stroke	25 (13)	18 (9)	0.2
Peripheral artery disease	19 (10)	19 (10)	0.87
Diabetes	74 (39)	46 (23)	<0.001
Chronic obstructive pulmonary disease	32 (17)	33 (17)	>0.99
Dementia	25 (14)	9 (5)	0.002
Cancer	19 (16)	13 (16)	>0.99
Lack of home care	6 (3)	6 (3)	>0.99
Physical parameters			
Resting heart rate on admission, bpm	100 (75–120)	85 (75–110)	<0.001
Resting heart rate at discharge, bpm	70 (65–80)	75 (70–80)	0.11
Systolic blood pressure on admission, mm Hg	140 (115–160)	135 (115–150)	0.07
Systolic blood pressure at discharge, mm Hg	123 (110–140)	120 (110–133)	0.12

TABLE 1 Baseline clinical characteristics of the study groups (continued from the previous page)

Parameter		2010–2011 (n = 191)	2016–2017 (n = 203)	*P* value
Causes of HF hospitalization				
Infections		55 (29)	74 (36)	0.11
Acute coronary syndrome		28 (15)	8 (4)	<0.001
Tachyarrhythmias		49 (26)	50 (25)	0.82
Other		30 (16)	21 (10)	0.13
Unknown reason		63 (33)	78 (38)	0.29
≥2 causes of HF exacerbation		51 (27)	47 (23)	0.48
No treatment compliance		38 (20)	49 (24)	0.33
Symptoms				
NYHA class III on admission		79 (42)	120 (59)	<0.001
NYHA class IV on admission		111 (58)	82 (41)	
Right ventricular HF symptoms		59 (31)	72 (35)	0.34
Left ventricular HF symptoms		185 (97)	199 (98)	0.53
Laboratory parameters				
Hemoglobin, g/dl		14 (12–15)	14 (12–15)	0.44
CRP, mg/l		11 (4–32)	7 (4–20)	0.03
Sodium, mmol/l		139 (137–141)	140 (138–142)	0.01
Glucose, mg/dl		132 (105–195)	117 (100–154)	0.01
High-sensitivity troponin T, ng/ml		0.03 (0.01–0.07)	0.03 (0.02–0.05)	0.04
LDL cholesterol, mg/dl		95 (73–115)	84 (61–101)	0.03
eGFR, ml/min/1.73 m^2	Total	62 (41–87)	68 (49–93)	0.04
	≥60	77 (53)	123 (62)	0.07
	50–59	18 (12)	27 (14)	
	30–49	36 (25)	39 (20)	
	<30	15 (10)	8 (4)	
Echocardiographic parameters				
LVEF, %	Total	30 (25–45)	35 (25–45)	0.19
	<40	117 (64)	123 (61)	0.86
	40–49	29 (16)	35 (17)	
	≥50	37 (20)	44 (22)	
Diastolic dysfunction degree	1	20 (32)	31 (21)	0.01
	2	23 (37)	92 (62)	
	3	14 (23)	19 (13)	
	Unspecified	5 (8)	6 (4)	
Left atrial diameter, cm		4.6 (4.3–5)	4.9 (4.5–5.3)	<0.001
Right ventricular systolic pressure, mm Hg		40 (25–45)	45 (34–55)	<0.001
Severe aortic valve defects		8 (4)	10 (5)	0.82
Severe mitral valve defects		40 (21)	27 (13)	0.08

Categorical variables are presented as number and percentage, and continuous variables, as median and interquartile range.

SI conversion factors: to convert creatinine to µmol/l, multiply by 0.6206; C-reactive protein to nmol/l, multiply by 9.524; glucose to mmol/l, multiply by 0.05 551, hemoglobin to mmol/l, multiply by 88.42; high-sensitivity troponin T to µg/l, multiply by 1; low-density lipoprotein cholesterol to nmol/l, multiply by 0.0259.

Abbreviations: CABG, coronary artery bypass grafting; CRP, C-reactive protein; eGFR, estimated glomerular filtration rate; HF, heart failure; LDL, low-density lipoprotein; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; PCI, percutaneous coronary intervention

TABLE 2 Treatment of the study patients

Parameter		2010–2011 (n = 191)	2016–2017 (n = 203)	*P* value
Hospitalization length, d, median (IQR)		7 (5–11)	7 (5–11)	0.41
Treatment during hospitalization				
Amine		17 (9)	9 (4)	0.1
Blood transfusion		6 (3)	12 (6)	0.23
Mechanical ventilation		12 (6)	11 (5)	0.83
Percutaneous revascularization		27 (14)	8 (4)	<0.001
Pharmacotherapy at discharge				
ACEIs / sartans	ACEIs / sartans	153 (86)	168 (84)	0.77
	ACEIs	123 (69)	147 (74)	0.36
	Sartans	30 (17)	21 (11)	0.1
MRAs	Any	90 (53)	97 (50)	0.68
	Spironolactone	84 (49)	50 (26)	<0.001
	Eplerenone	6 (4)	47 (24)	<0.001
Other medications	β-Blockers	155 (91)	178 (92)	0.72
	Statins	116 (68)	130 (67)	0.91
	Diuretics	160 (94)	183 (94)	0.83
	Potassium	77 (45)	137 (71)	<0.001
	Antiplatelet agents	78 (46)	59 (30)	0.003
	VKA / LMWH	97 (51)	65 (32)	< 0.001
	NOACs	0	73 (36)	< 0.001
	Digoxin	32 (19)	29 (15)	0.40
	Amiodarone	34 (20)	23 (12)	0.04
	Calcium channel blockers	37 (22)	30 (15)	0.14
Electrotherapy				
ICD and CRT-D		42 (22)	62 (31)	0.82
Resynchronization devices (CRT-D and CRT-P)		15 (8)	22 (11)	0.71
Discharge				
At home		164 (93)	180 (91)	0.49
To another hospital		7 (4)	11 (6)	
To a nursing home		1 (1)	3 (2)	

Data are presented as number (percentage) of patients unless otherwise indicated.

Abbreviations: ACEIs, angiotensin-converting enzyme inhibitors; CRT-D, cardiac resynchronization therapy defibrillator; CRT-P, cardiac resynchronization therapy pacemaker; ICD, implantable cardioverter-defibrillator; LMWH, low-molecular-weight heparin; MRAs, mineralocorticoid receptor antagonists; NOACs, non–vitamin K antagonist oral anticoagulants; VKA, vitamin K antagonist

anticoagulants (NOACs) (from 0% to 36%). We also observed a significant reduction in the use of amiodarone (from 20% to 12%) and an increase in potassium supplementation (from 45% to 71%).

Electrotherapy In the 2010–2011 group, 42 patients (22%) had an implantable cardioverter-defibrillator (ICD; including ICDs with cardiac resynchronization therapy); between 2016 and 2017, that number (62 patients [31%]) did not increase significantly (TABLE 2). Resynchronization devices (cardiac resynchronization therapy defibrillators [CRT-Ds] and cardiac resynchronization therapy pacemakers [CRT-Ps]) were implanted in 15 (8%) and 22 (11%) patients in the years 2010 to 2011 and 2016 to 2017, respectively (P = 0.71). A detailed description of the above data is presented in Supplementary material, *Table S1*. In patients with an indication for ICD (including CRT-D) implantation (LVEF ≤35%), only 37% (42 out of 115 patients) of the patients hospitalized between 2010 and

TABLE 3 Results of Cox proportional hazard regression analysis for the analyzed parameters (with the prespecified cutoff values for continuous variables) as a predictor of all-cause mortality

Parameter	Univariate analysis		*P* value
	HR	95% CI	
Male sex	1.44	1.13–1.95	0.04
Age ≥72 y	2.49	1.76–3.52	0.02
BMI ≤27 kg/m^2	2.04	1.4–2.98	<0.001
Hypertension	1.55	1.13–2.14	0.01
Stroke	1.65	1.06–2.58	0.03
Dementia	2.85	1.83–4.42	<0.001
Cancer	2.54	0.93–6.95	0.07
No home care	2.72	1.33–5.55	0.01
Systolic blood pressure ≤121 mm Hg	1.65	1.13–2.4	0.01
Infection as the cause of HF exacerbation	1.84	1.02–3.32	0.04
NYHA class III at discharge	1.81	1.23–2.67	0.003
Right ventricular HF symptoms	1.43	1.03–1.98	0.03
Hemoglobin ≤14.8 g/dl	1.54	1.02–2.3	0.04
CRP ≥32 mg/l	2.05	1.38–3.03	<0.001
Sodium ≤139 mmol/l	1.56	1.11–2.21	0.01
Glucose ≥119 mg/dl	1.8	1.24–2.61	0.002
High-sensitivity troponin T ≥0.0325 ng/ml	1.90	1.32–2.73	<0.001
LDL cholesterol ≥79 mg/dl	1.86	1.06–3.26	0.03
eGFR ≤49 ml/min/1.73 m^2	2.77	1.93–3.99	<0.001
NT-proBNP ≥5631 pg/ml	1.98	1.21–3.26	0.01
LVEF <40%	5.13	2.51–10.51	<0.001
Catecholamines during hospitalization	2.81	1.70–4.67	<0.001
Blood transfusion during hospitalization	2.49	1.38–4.49	0.003
Mechanical ventilation during hospitalization	3.60	2.17–5.98	0.002
Absence of β-blockers at discharge	2.66	1.63–4.34	<0.001
Absence of ACEIs / sartans at discharge	2.07	1.37–3.13	<0.001
Absence of MRAs at discharge	1.52	1.06–2.17	0.02
Discharge to a hospital or nursing home	2.95	1.69–5.14	<0.001
Prolonged hospitalization ≥9 days	1.88	1.36–2.6	0.002
Number of recurrent hospitalizations ≥2	1.98	1.43–2.75	0.002

SI conversion factors: to convert N-terminal fragment of the prohormone brain natriuretic peptide to pmol/l, multiply by 0.118; others, see TABLE 1.

Abbreviations: BMI, body mass index; HR, hazard ratio; NT-proBNP, N-terminal fragment of the prohormone brain natriuretic peptide; others; see TABLES 1 and 2

2011 and 56% (62 out of 110 patients) of the patients hospitalized in the years 2016 to 2017 underwent the procedure.

Prognosis In-hospital mortality did not differ between the analyzed groups, although there was a slight trend towards reduced rates in the years 2016 and 2017. There was a reduction in overall mortality among patients hospitalized between 2016 and 2017 compared with those hospitalized between 2010 and 2011 (44% vs 33%; $P = 0.03$). On the other hand, the number of rehospitalizations due to HF exacerbation increased from 26% to 41% ($P < 0.001$) (Supplementary material, *Table S2*). In the Cox proportional hazard regression analysis, we identified numerous clinical, laboratory, and treatment-related variables, which predicted all-cause mortality (TABLE 3) and rehospitalizations due to HF exacerbation (TABLE 4). For continuous variables, we based those calculations on cutoff values prespecified in ROC analysis (Supplementary material, *Table S3*). Male sex, low systolic blood pressure, symptoms of right HF, and renal dysfunction constituted independent risk factors for the primary endpoint, whereas symptoms of right HF, renal dysfunction, LVEF below 24%, and low systolic blood pressure independently predicted the secondary endpoint (TABLE 5).

DISCUSSION This study was a single-center, retrospective analysis of patients hospitalized for HF exacerbation. Importantly, our data came from a regional district hospital, which fills the gap in previous publications on large clinical trials.

Previous studies have reported ischemic heart disease as the most common cause of HF exacerbation requiring hospitalization,[1,19] affecting about 70% of the European population,[20] including two-thirds of patients with reduced LVEF.[21] Our results are in line with these statistics. Of note, the percentage of patients with a history of myocardial infarction was higher among those hospitalized between 2010 and 2011 (52%) compared with those hospitalized in the years 2016 to 2017 (41%; $P = 0.03$). This finding is consistent with the general trend in the management of acute coronary syndrome over the last decade, which has resulted in earlier hospital admission and application of invasive, preventive, and pharmacological interventions.[16] The most common comorbidities in patients hospitalized for HF exacerbation include diabetes, arterial hypertension, and atrial fibrillation, as shown by large global registries.[13,22,23] The distribution of these diseases in our regional hospital population was similar (TABLE 1).

Laboratory characteristics revealed that patients hospitalized between 2016 and 2017 had higher serum sodium levels and glomerular filtration rates yet lower C-reactive protein, glucose, troponin T, and low-density lipoprotein cholesterol levels (TABLE 1). Indirectly, these results may reflect the quality of outpatient treatment of patients 10 years ago, which has undoubtedly improved in recent years after introducing the latest HF guidelines. Patients hospitalized between 2016 and 2017 were more frequently classified as

TABLE 4 Results of Cox proportional hazard regression analysis for the analyzed parameters (with the prespecified cutoff values for continuous variables) as a predictor of rehospitalization due to heart failure exacerbation

Parameter	Univariate analysis		*P* value
	HR	95% CI	
Atrial fibrillation / flutter	1.48	1.05–2.08	0.03
Chronic obstructive pulmonary disease	1.75	1.17–2.64	0.01
Lack of home care	2.84	1.25–6.45	0.01
Resting heart rate ≥86 bpm	1.54	1.02–2.33	0.04
Systolic blood pressure at discharge ≤111 mm Hg	2	1.39–2.91	<0.001
Lack of treatment compliance	1.6	1.09–2.34	0.02
Right ventricular HF symptoms	1.54	1.09–2.18	0.02
CRP ≥2.9 mg/l	1.66	1.12–2.47	0.01
Glucose ≥222 mg/dl	2.29	1.16–4.51	0.02
High-sensitivity troponin T ≥0.0175 ng/ml	1.69	1.10–2.58	0.02
LDL cholesterol ≥110 mg/dl	3.56	1.54–8.21	0.003
eGFR <30 ml/min/1.73 m^2	1.54	1.04–2.27	0.03
NT-proBNP ≥8729.5 pg /ml	2.3	1.43–3.7	<0.001
LVEF ≤24%	1.92	1.34–2.76	<0.001
Mechanical ventilation during hospitalization	2.09	1.02–4.27	0.04

SI conversion factors: see TABLES 1 and 3

Abbreviations: see TABLES 1 and 3

TABLE 5 Results of multivariable Cox proportional hazard regression analysis for the prespecified cutoff values of the analyzed parameters as predictors of all-cause 2-year mortality and rehospitalization due to heart failure exacerbation

Parameter		HR	95% CI	*P* value
All-cause mortality	Male sex	2.62	1.82–3.78	<0.001
	Systolic blood pressure <121 mm Hg	1.8	1.27–2.55	<0.001
	Right ventricular HF symptoms	1.38	1.01–1.91	0.045
	eGFR ≤49 ml/min/1.73 m^2	2.31	1.58–3.38	<0.001
Rehospitalization due to HF exacerbation	Systolic blood pressure ≤111 mm Hg	1.77	1.2–2.61	0.004
	Right ventricular HF symptoms	1.59	1.11–2.27	0.01
	eGFR ≤30 ml/min/1.73 m^2	2.18	1.25–3.8	0.01
	LVEF ≤24%	1.68	1.01–2.8	0.045

Abbreviations: see TABLES 1 and 3

having NYHA class III more often than class IV, characterized by a larger left atrium, features of diastolic dysfunction, and higher right ventricular systolic pressure, which is consistent with the general trend in the literature.[24,25]

Our findings clearly show a change in the management of patients admitted in the years 2016 to 2017 in comparison with those hospitalized between 2016 and 2017, with a reduction in the frequency of use of sartans, antiplatelet drugs, VKAs, and low-molecular-weight heparin in favor of a significant increase in the use of eplerenone and NOACs (TABLE 2). This could be partially a consequence of the implementation of the 2016 HF guidelines,[6] as well as of the recommendation to use NOACs rather than VKAs as the first-line drugs to prevent thromboembolic events in atrial fibrillation and a move away from the routine use of aspirin for that purpose.[26] However, those guidelines could probably affect only some patients owing to the inevitable adaptation period after introducing new guidelines in clinical practice, the length of which is difficult to estimate. Although the use of spironolactone was lower and of eplerenone higher in the years 2016 to 2017, the frequency of mineralocorticoid receptor antagonist (MRA) use was similar in both study groups: 50% in the 2016–2017 group and 53% in the 2010–2011 group (TABLE 2). Those rates seem low despite better renal function and a higher rate of potassium supplementation in the patients hospitalized between 2016 and 2017, which could be a complex consequence of not only the frequency of MRA use but also numerous other components. What is more, a relatively low rate of MRA use in both study periods could be explained by the distribution of LVEF in the whole patient group. The percentage of low LVEF was only 64% in 2010 to 2011, and 61% in 2016 to 2017; there are no specific guidelines for the treatment of patients with higher LVEF.

The ESC guidelines recommend the implantation of a cardioverter-defibrillator and resynchronization therapy in patients with reduced LVEF to decrease mortality in HF.[6,10] In our study, those treatments were used infrequently in patients with reduced LVEF, particularly resynchronization therapy, and only a slight increase in the procedure use was noted in the years 2016 to 2017 compared with 2010 to 2011 (Supplementary material, *Table S1*). This is undoubtedly due to the noticeably low financial support from the Polish National Health Fund for district hospitals.

According to German Federal Ministry of Health registries,[27] in-hospital death due to HF was relatively high, amounting to 9.3% in 2013. That rate was similar to the rate of in-hospital mortality in our patients hospitalized in both study periods (Supplementary material, *Table S2*). The median length of hospitalizations due to HF exacerbation in our study was similar to the upper limit reported in large multicenter studies from the United States and Europe.[28,29]

The rate of posthospitalization mortality in patients with HF reported by the Polish National Health Fund data analysis is about 11% annually.[3] The mortality of patients hospitalized for

HF is several-fold higher and has been reported to be as high as 30% at the annual follow-up after hospitalization.[10] According to data from the United States National Center for Health Statistics, the age-adjusted rate for HF-related deaths decreased after 2000.[30] The results of our study seem to confirm this trend (Supplementary material, *Table S2*). We observed a significant reduction in the 2-year mortality rate from 44% to 33% (P = 0.03). These differences are most likely a consequence of the improved treatment of patients with HF. However, it should be noted that, despite this reduction, mortality remains high. The decrease in all-cause mortality was associated with a greater number of rehospitalizations due to HF exacerbation, which is in line with data from previous studies.[1,10,30]

Several relevant risk factors for poorer HF prognosis have been reported and those were confirmed in our study.[13,31-39] The MADIT II (Multicenter Automatic Defibrillator Implantation Trial II) cohort analysis identified renal failure as one of the strongest predictors of poor prognosis.[35] Gheorghiade et al[36] and Ambrosy et al[37] listed renal failure and low systolic blood pressure among factors influencing the prognosis of patients hospitalized for HF. Our findings are also consistent with those from a meta-analysis by Ouwerkerk et al,[13] which included over 9 million patients and reported among others, renal dysfunction, hypertension, LVEF, and male sex to be the strongest predictors of poor prognosis. Previous studies have also consistently demonstrated increased mortality in patients with right ventricular dysfunction.[38] The independent risk factors for all-cause mortality and rehospitalization due to HF exacerbation identified in our study are in line with the findings cited above. Factors that independently predicted all-cause mortality encompassed male sex, symptoms of right ventricular HF, significant renal dysfunction, and systolic blood pressure below 121 mm Hg (TABLE 5). Regarding the latter parameter, a similar systolic blood pressure value was mentioned in the latest European guidelines for the management of hypertension.[40] It has been identified as a risk factor in relatively young individuals (<65 years old) without dominant HF. Factors that independently predicted rehospitalization due to HF exacerbation included symptoms of right HF, significant renal dysfunction, HF with LVEF below 24%, and systolic blood pressure lower than 111 mm Hg (TABLE 5).

Limitations Our study had several limitations. First, it was a retrospective analysis, and its results should thus be interpreted with caution. The availability of some data and parameters in patients' medical records was limited (including the lack of information about the exact time of medication discontinuation among patients who did not comply with treatment). Additionally, we could not check the patients' exact treatment before the first hospitalization, as well as the continuation of the treatment after the first hospitalization. We did not check the doses of medications at discharge and whether they were optimized during the 2-year follow-up, which limits our knowledge in this area. Two patients from the 2010–2011 period were enrolled again between 2016 and 2017; however, after the exclusion of those patients from statistical analysis, the results did not change. Our study was a small, single-center study, which is the next limitation, although some benefits associated with the single-center design have been identified (including laboratory and echocardiographic data that were collected from the same laboratory, obtained mainly by the same experts, which reduced interobserver variability). The next remarkable limitation of our study was the lack of brain natriuretic peptide measurements in most study patients hospitalized between 2010 and 2011. However, this is representative of real-life clinical challenges in a regional hospital, which may complicate the timely diagnosis of HF.

Conclusions Our study revealed that the prognosis of patients hospitalized for HF decompensation in a regional district hospital is poor. The implementation of the latest ESC guidelines resulted in some improvement in the clinical characteristics and treatments at discharge, which probably led to a reduction in the risk of all-cause mortality. However, the low rate of implantable electronic device use and the high rate of rehospitalizations due to HF exacerbation need to be addressed. Patients at the highest risk of death and rehospitalization require further intensification of outpatient and inpatient therapy.

SUPPLEMENTARY MATERIAL

Supplementary material is available at www.mp.pl/kardiologiapolska.

ARTICLE INFORMATION

CONTRIBUTION STATEMENT LD-S and MD conceived the concept of the study. MD and LD-S contributed to the study design. MD was involved in data collection. MD, LD-S, PM, and MŚ analyzed the data. MD, LD-S, MŚ, and PM wrote the manuscript. GR revised the manuscript. All authors edited and approved the final version of the manuscript.

CONFLICT OF INTEREST None declared.

HOW TO CITE Dobrowolska M, Miękus P, Świątczak M, et al. Two-year prognosis of patients hospitalized for decompensated heart failure in a district general hospital. Kardiol Pol. 2021; 79: 302-310. doi:10.33963/KP.15763

REFERENCES

1 Ziaeian B, Fonarow GC. Epidemiology and aetiology of heart failure. Nat Rev Cardiol. 2016; 13: 368-378.

2 Heidenreich PA, Albert NM, Allen LA, et al. Forecasting the impact of heart failure in the United States. A policy statement from the American Heart Association. Circ Heart Fail. 2013; 6: 606-619.

3 Gierczyński J, Gryglewicz J, Karczewicz E, Zalewska H. Heart failure – analysis of economic and social costs [in Polish]. Warsaw: Lazarski University; 2013.

4 Heart failure in Poland – the 2016 report [in Polish]. Information materials of the PCS Heart Failure Section. http://www.niewydolnosc-serca.pl/barometr.pdf. Accessed July 15, 2018.

5 Foster M. HF app to support self-care among community dwelling adults with HF: a feasibility study. Appl Nurs Res. 2018; 44: 93-96.

6 Ponikowski P, Voors AA, Anker SD, et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur J Heart Fail. 2016; 18: 891-975.

7 Berkovitch A, Maor E, Sabbag A, et al. Precipitating factors for acute heart failure hospitalization and long-term survival. Medicine (Baltimore). 2015; 94: e2330.

8 Lelonek M, Książczyk M, Pawlak A, et al. Heart failure management in Polish medical centers during the coronavirus disease 2019 pandemic: results of a survey. Kardiol Pol 2020; 78: 1035-1038.

9 Raj L, Maidman SD, Adhyaru BB. Inpatient management of acute decompensated heart failure. Postgrad Med J. 2020; 96: 33-42.

10 Lelonek M. Heart failure – the post-discharge period as the key element of the management [in Polish]. Folia Cardiol. 2018; 13: 371-377.

11 OECD (2015). Avoidable hospital admissions. In: OECD (2015). Health at a glance 2015: OECD indicators. Paris: OECD Publishing; 2015: 132-133. https://read.oecd-ilibrary.org/social-issues-migration-health/health-at-a-glance-2015_health_glance-2015-en#page1. Accessed November 4, 2015.

12 Krim SR, Campbell PT, Desai S, et al. Management of patients admitted with acute decompensated heart failure. Ochsner J. 2015; 15: 284-289.

13 Ouwerkerk W, Voors AA, Zwinderman AH, et al. Factors influencing the predictive power of models for predicting mortality and / or heart failure hospitalization in patients with heart failure. J Am Coll Cardiol Heart Fail. 2014; 2: 429-436.

14 O'Connor CM, Abraham WT, Albert NM, et al. Predictors of mortality after discharge in patients hospitalized with heart failure: an analysis from the Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure (OPTIMIZE-HF). Am Heart J. 2008; 156: 662-673.

15 McMurray JJ, Packer M, Desai AS, et al. Dual angiotensin receptor and neprilysin inhibition as an alternative to angiotensin-converting enzyme inhibition in patients with chronic systolic heart failure: rationale for and design of the Prospective comparison of ARNI with ACEi to Determine Impact on Global Mortality and morbidity in Heart Failure trial (PARADIGM-HF). Eur J Heart Fail. 2013; 15: 1062-1073.

16 Gerber Y, Weston SA, Jiang R, et al. The changing epidemiology of myocardial infarction in Olmsted County, Minnesota, 1995-2012. Am J Med. 2015; 128: 144-151.

17 Gerber Y, Weston SA, Redfield MM, et al. A contemporary appraisal of the heart failure epidemic in Olmsted County, Minnesota, 2000–2010. JAMA Intern Med. 2015; 175: 996-1004.

18 Hummel A, Empe K, Dorr M, et al. De novo acute heart failure and acutely decompensated chronic heart failure. Dtsch Arztebl Int. 2015; 112: 298-310.

19 Bautista PS, Martel AC, Bodas OA, et al. Precipitating factors of heart failure admission: differences related to age and left ventricular ejection fraction. Int J Cardiol. 2016; 219: 150-155.

20 Ostręga M, Gierlotka MJ, Słonka G, et al. Clinical characteristics, treatment, and prognosis of patients with ischemic and nonischemic acute severe heart failure. Analysis of data from the COMMIT-AHF registry. Pol Arch Intern Med. 2017; 127: 328-335.

21 Pyka L, Hawranek M, Tajstra M, et al. Complete percutaneous revascularisation feasibility in ischaemic heart failure is related to improved outcomes: insights from the COMMIT-HF registry. Kardiol Pol. 2017; 75: 453-461.

22 Echouffo-Tcheugui JB, Xu H, DeVore AD, et al. Temporal trends and factors associated with diabetes mellitus among patients hospitalized with heart failure: findings from get with the guidelines-heart failure registry. Am Heart J. 2016; 182: 9-20.

23 Kenny HC, Abel ED. Heart failure in type 2 diabetes mellitus: impact of glucose lowering agents, heart failure therapies and novel therapeutic strategies. Circ Res. 2019; 124: 121-141.

24 Kroch E, Duan M, Martin J, et al. patient factors predictive of hospital readmissions within 30 days. J Healthc Qual. 2016; 38: 106-115.

25 Aschauer S, Kammerlander AA, Zotter-Tufaro C, et al. The right heart in heart failure with preserved ejection fraction: insights from cardiac magnetic resonance imaging and invasive haemodynamics. Eur J Heart Fail. 2016; 18: 71-80.

26 Kirchhof P, Benussi S, Kotecha D, et al. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. Eur Heart J. 2016; 37: 2893-2962.

27 Christ M, Störk S, Dörr M, et al. Heart failure epidemiology 2000–2013: insights from the German Federal Health Monitoring System. Eur J Heart Fail. 2016; 18: 1009-1018.

28 Farmakis D, Parissis J, Lekakis J, et al. Acute heart failure: epidemiology, risk factors, and prevention. Rev Esp Cardiol (Engl Ed). 2015; 68: 245-248.

29 Moriyama H, Kohno T, Kohsaka S, et al. Length of hospital stay and its impact on subsequent early readmission in patients with acute heart failure: a report from the WET-HF Registry. Heart Vessels. 2019; 34: 1777-1788.

30 Ni H, Xu J. Recent trends in heart failure-related mortality: United States, 2000–2014. NCHS Data Brief. 2015; 231: 1-8.

31 Kaufmann D, Szwoch M, Kwiatkowska J, et al. Global longitudinal strain can predict heart failure exacerbation in stable outpatients with ischemic left ventricular systolic dysfunction. PLoS One. 2019; 14: e0225829.

32 Asano R, Kajimoto K, Oka T, et al. Association of New York Heart Association functional class IV symptoms at admission and clinical features with outcomes in patients hospitalized for acute heart failure syndromes. Int J Cardiol. 2017; 230: 585-591.

33 Moita B, Marques AP, Camacho AM, et al. One-year rehospitalisations for congestive heart failure in Portuguese NHS hospitals: a multilevel approach on patterns of use and contributing factors. BMJ Open. 2019; 9: e031346.

34 Ayalon-Dangur I, Rudman Y, Shochat T, et al. Elevated blood pressure during emergency departments visit is associated with increased rate of hospitalization for heart failure: a retrospective cohort study. J Clin Hypertens (Greenwich). 2018; 20: 98-103.

35 Khoo CY, Allen JC, Chia SY, et al. Mortality outcome and predictive risk factors for death in patients with heart failure and reduced ejection fraction who declined implantable cardioverter defibrillator implantation in Singapore. J Arrhythm. 2018; 34: 536-540.

36 Gheorghiade M, Vaduganathan M, Ambrosy A, et al. Current management and future directions for the treatment of patients hospitalized for heart failure with low blood pressure. Heart Fail Rev. 2013; 18: 107-122.

37 Ambrosy AP, Vaduganathan M, Mentz RJ, et al. Clinical profile and prognostic value of low systolic blood pressure in patients hospitalized for heart failure with reduced ejection fraction: insights from the Efficacy of Vasopressin Antagonism in Heart Failure: Outcome Study with Tolvaptan (EVEREST) trial. Am Heart J. 2013; 165: 216-225.

38 Mohammed SF, Hussain I, Abou-Ezzeddine OF, et al. Right ventricular function in heart failure with preserved ejection fraction. Circulation. 2014; 130: 2310-2320.

39 Vergaro G, Januzzi JL, Solal AC, et al. NT-proBNP prognostic value is maintained in elderly and very elderly patients with chronic systolic heart failure. Int J Cardiol. 2018; 271: 324-330.

40 Williams B, Mancia G, Spiering W, et al. 2018 ESC/ESH Guidelines for the management of arterial hypertension. Eur Heart J. 2018; 39: 3021-3104.