

# Risk factors for poor prognosis in heart failure with particular attention to the elderly population

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## Abstract

**Background:** Heart failure (HF) is a leading cause of poor outcome. Age is considered one of the most critical risk factors for both the incidence and prognosis of HF. Therefore we aimed to assess the predictors of poor prognosis in HF patients with particular attention to the elderly population. **Material and methods:** We retrospectively enrolled patients hospitalized due to HF exacerbation during 2016-2017 (203 patients). The end-points were all-cause mortality and emergency rehospitalizations within a two-year follow-up period. A detailed analysis was performed in the subgroups of patients younger and older than 65 years old. **Results:** 121 (60%) patients experienced the end-points. Age, low systolic blood pressure, NYHA class IV, right ventricle HF symptoms, high C-reactive protein, troponin, NT-proBNP, hyponatremia, catecholamine therapy and mechanical ventilation during hospitalization independently predicted the end-points. The elderly were characterized by a higher incidence of concomitant diseases and HF with moderately reduced or preserved LVEF, worse laboratory parameters and pharmacological treatment, as well as worse prognosis. **Conclusion:** The prognosis of patients hospitalized due to HF, mainly the elderly, is poor. Simple clinical parameters could be useful in further decision-making regarding the intensification of their treatment.

**Keywords:** heart failure · risk factors · prognosis · elderly

## Citation

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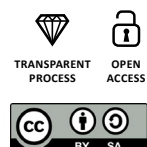
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## Introduction

Heart failure (HF) is a continually growing global pandemic [1]. Despite significant advancements in the pharmacological and invasive treatment of HF, based on the widespread use of implantable cardioverter-defibrillators and resynchronization therapy to reduce mortality, the morbidity and mortality are still high [2-4]. HF exacerbation is the leading cause of hospital admissions [5], thus a considerable health burden for patients and the health care system [6-7]. Patients hospitalized due to HF exacerbation are known to have the worst prognosis [1, 4]. Therefore, assessing such patients and identifying predictors that affect the prognosis is critical from a clinical point of view. Age is considered one of the most important risk factors for HF incidence and prognosis [8-9]. The prevalence of HF increases rapidly with age: it doubles from 6% in people aged 60-79 years old to about 14% in those aged  $\geq 80$  years old; [10] respect 4-5% of individuals 45 years and older [9]. The clinical trials to date are quite poor in the elderly population [11-13]. However, recent data from the EuroHeart Failure Survey shows that older patients with HF have poor short-term survival and are not treated according to the HF guidelines [11, 14]. Given all of the above, we aimed to assess the predictors of poor prognosis in patients hospitalized with HF with particular attention to the elderly population.

## Material and methods

### Patients selection

This study is a sub-analysis of our retrospective project [15] of all patients hospitalized with a diagnosis of acutely decompensated chronic HF and new-onset acute HF [16] in at a single cardiology department (St. Vincent Hospital in Gdynia, Poland) during 2016-2017. Further analysis included: the patient's biometric parameters, the medical history available in the documentation (with particular emphasis on comorbidities, condition of the coronary vessels, implanted devices, the treatment so far), physical examination findings documented during hospitalization, laboratory results, electrocardiography and echocardiography [15]. The data was obtained from the hospital's medical records and electronic patient records. Exclusion criteria were as follows: patients  $< 18$  years old, NYHA functional class I and II on admission, and no clinical signs of HF. All patients were followed up for two years. The *composite end-point* included: all-cause mortality and emergency rehospitalizations (including those due to HF exacerbation). Additional analyses were carried out differentiating between patients younger and older than 65 years of age. The study protocol was approved by the Local Ethics Committee of the Medical University of Gdańsk (decision number NKBBN/619/2018). All data we analyzed

was collected during standard, routine clinical practice, therefore it was not required to obtain the participants' written and informed consent for anonymized storage of information and its use for research.

### Statistical analysis

Continuous data are presented as the median (25<sup>th</sup>-75<sup>th</sup> percentiles), whereas categorical variables as numbers (n) and percentages (%). Comparisons between the patients were made with U Mann-Whitney's test or the Fisher's exact test due to abnormally distributed variables. An association between the analyzed parameters and the end-point was assessed using the univariate and multivariate Cox hazard models. The accuracy of pre-specified cut-off values for the analyzed parameters and their association as potential predictors of the study end-point was determined by area under (AUC) the receiver-operating characteristic (ROC) curve. All the results were considered statistically significant with  $p \leq 0.05$ . The statistical analysis was performed using the Statistica 12.0 software (*StatSoft, Tulsa OK, USA*) and R 2.15.2 (R Project).

### Results

We included 203 patients hospitalized due to HF exacerbation in the years 2016-2017. Within a two-year observation period, 121 instances of composite end-points (all-cause mortality and emergency rehospitalizations) were documented.

### Clinical, laboratory, and echocardiographic findings

Most of the patients included in the study were men (Table 1). Patients who experienced end-points were older (median age 73 versus 68 years old in group without endpoints,  $p = 0.046$ ), they more frequently had a history of atrial fibrillation/flutter (44% vs. 18%,  $p < 0.001$ ) and diabetes (29% vs. 13%,  $p = 0.010$ ), were also more likely to undergo coronary revascularization (47% vs. 30%,  $p = 0.020$ ) and had lower systolic blood pressure (SBP) at discharge (median 120 vs. 128 mmHg,  $p = 0.047$ ). In addition they had worse renal function indices, lower sodium values, higher troponin and natriuretic peptide levels (Table 1). In the echocardiographic assessment, these patients were characterized by more advanced left ventricular diastolic dysfunction and a trend towards worse systolic function (Table 1). There were no differences in pharmacotherapy; moreover, it should be emphasized that the majority of patients were treated according to the current guidelines [8]:  $> 90\%$  of patients received a beta-blocker,  $> 80\%$  were treated with an ACE-inhibitor or sartans; however the frequency of spironolactone/epplerenone use was lower than suggested in the guidelines (Table 1).

Table 1. Baseline clinical characteristics of the study patients according the end-point

Parameters	End-point (-) n = 82	End-point (+) n = 121	p
Male, n (%)	56 (68)	88 (73)	0.531
Age (years)	68 (61-79)	73 (64-81)	<b>0.046</b>
<b>Medical history</b>			
Coronary artery disease, n (%)	45 (56)	81 (68)	0.135
Revascularization (PCI/CABG), n (%)	25 (30)	57 (47)	<b>0.020</b>
ICD (including CRT-D)	14 (17)	30 (25)	0.212
Atrial fibrillation/flutter, n (%)	15 (18)	53 (44)	<b>&lt; 0.001</b>
Hypertension, n (%)	28 (34)	47 (39)	0.554
Diabetes mellitus, n (%)	11 (13)	35 (29)	<b>0.010</b>
Cancer, n (%)	2 (5)	11 (26)	0,016
<b>Cause of hospitalization</b>			
Infections, n (%)	24 (29)	50 (41)	0.102
Acute coronary syndrome, n (%)	2 (2)	6 (5)	0.478
Tachyarrhythmias, n (%)	20 (24)	30 (25)	1.000
Unknown reason, n (%)	38 (46)	40 (33)	0.077
Other, n (%)	9 (11)	12 (10)	0.818
The length of hospitalisation (days)	7 (5-9)	8 (5-12)	<b>0.041</b>
<b>Clinical and diagnostic parameters</b>			
Resting heart rate (beats /min)	83 (75-110)	90 (75-110)	0,225
SBP (mmHg)	128 (115-133)	120 (109-131)	<b>0.047</b>
NYHA class IV at admission, n (%)	27 (33)	55 (46)	0.080
Right ventricle HF symptoms at admission, n (%)	20 (24)	52 (43)	<b>0.007</b>
Hemoglobin (g/dl)	14 (12-15)	13 (12-15)	0.186
C-reactive protein (mg/l)	7 (3-16)	8 (4-22)	0.105

Sodium (mmol/l)	141 (139-142)	140 (137-142)	<b>0.030</b>
Glucose (mg/dl)	110 (98-141)	123 (105-163)	0.071
High-sensitivity troponin T (ng/ml)	0.042 (0.017-0.043)	0.105 (0.021-0.076)	<b>&lt; 0.001</b>
Creatinine (mg/dl)	1.24 (0.81-1.32)	1.25 (0.91-1.51)	0.072
NT-proBNP (ng/l)	2432 (732-6115)	5170 (2474-10449)	<b>&lt; 0.001</b>
<b>Echocardiographic parameters</b>			
LVEF (%)	37 (25-50)	33 (23-45)	0.061
LVEF < 40, n (%)	44 (54)	79 (66)	0.202
LVEF 40-49, n (%)	16 (20)	19 (16)	
LVEF ≥ 50, n (%)	22 (27)	22 (18)	
Diastolic dysfunction 2/3 °, n (%)	39 (64)	72 (82)	<b>0.032</b>
Left atrium diameter (cm)	4.84 (4.4-5.3)	5.04 (4.6-5.4)	0.085
Right ventricular systolic pressure increased, n (%)	64 (82)	115 (97)	<b>&lt; 0.001</b>
<b>In-hospital treatment</b>			
Catecholamine, n (%)	1 (1)	8 (7)	0.087
Mechanical ventilation, n (%)	3 (4)	9 (7)	0.367
<b>Treatment at discharge</b>			
ACE-inhibitor/ Sartans, n (%)	73 (89)	95 (81)	0.166
Spirolactone / Eplerenone, n (%)	43 (52)	54 (48)	0.663
Beta-adrenolytics, n (%)	76 (93)	102 (91)	0.795
Statins, n (%)	50 (61)	80 (71)	0.164
Diuretics, n (%)	75 (91)	108 (96)	0.208
Potassium, n (%)	56 (68)	81 (72)	0.633
Antiplatelet therapy, n (%)	20 (24)	39 (35)	0.155
NOAC, VKA, LMWH, n (%)	58 (71)	79 (71)	1.000

Digoxin, n (%)	9 (11)	20 (18)	0.224
Amiodarone, n (%)	9 (11)	14 (13)	0.825

Categorical variables are presented as number and percentage. Continuous variables are presented as median and interquartile range. P values of < 0.05 are considered significant.

ACE-inhibitor – angiotensin converting enzyme inhibitor; CABG – coronary artery bypass grafting; CRT-D – cardiac resynchronization therapy defibrillator; ICD – implantable cardioverter-defibrillator; LMWH – low molecular weight heparin; LVEF – left ventricular ejection fraction; NOAC – novel oral anticoagulants; NT – proBNP-N-terminal pro brain natriuretic peptide; NYHA – New York Heart Association; PCI – percutaneous coronary intervention; SBP – systolic blood pressure; VKA – vitamin K antagonists.

Conversion factors to SI units are as follows: for creatinine mg/dl → umol/L: 0.6206; for CRP mg/l → nmol/L, 9.524; for glucose mg/dl → mmol/L, 0.05551, for hemoglobin g/dl → mmol/L, 88.42; for high-sensitivity troponin T ng/ml → μg/L, 1.0; for NT-proBNP ng/l → pmol/L, 0.118

### The predictors of the end-points

Table 2 presents the pre-specified on ROC curve analysis cut-off values for continuous variables with the highest discriminatory power in predicting the end-points (Table 2). In the Cox proportional hazard regression analysis, we revealed statistically significant clinical and laboratory variables,

which predicted the end-points: age ≥ 73 years old, lower SBP (≤ 120 mmHg), NYHA class IV on admission, right-sided HF symptoms, C-reactive protein ≥ 31.4(mg/l), sodium ≤ 137 mmol/l, troponin level ≥ 0.044 ng/ml, NT-proBNP level ≥ 2453 ng/l, catecholamine use and mechanical ventilation during hospitalization (Table 3).

**Table 2. Prognostic accuracy of the pre-specified cut-off values for analyzed parameters as predictors of composite end-points during the follow-up**

Parameters	AUC	Characteristics (95% CI)		Predictive Value (95% CI)	
		Sensitivity (%)	Specificity (%)	Positive (%)	Negative (%)
Age ≥ 73 years old	0.62	66	52	48	69
SBP ≤ 120 mmHg	0.58	70	50	47	73
C-reactive protein ≥ 31.4 mg/l	0.56	93	21	42	83
Sodium ≤ 137 mmol/l	0.59	95	23	45	87
High-sensitivity troponin T ≥ 0.044 ng/ml	0.64	79	45	49	76
Creatinine ≥ 1.15 mg/dl	0.58	70	44	46	68
NT-proBNP ≥ 2453 ng/l	0.67	51	75	58	69

Abbreviations: AUC – Area Under Curve; CI – confidence interval; other: see Table 1

**Table 3. Univariate and multivariate Cox proportional hazard regression as a predictor of composite end-point )**

Parameters	Univariate analysis		Multivariate analysis	
	HR (95% CI)	p	HR (95% CI)	p
Age ≥ 73 years	1.49 (1.04-2.13)	0.028	1.89 (1.24-2.88)	<b>0.003</b>
Atrial fibrillation / flutter	1.65 (1.15-2.37)	0.007	-	-
Cancer	2.48 (1.24-4.96)	0.010	-	-
SBP ≤ 120 mmHg	1.52 (1.01-2.29)	0.044	1.65 (1.09-2.49)	<b>0.018</b>
NYHA class IV at admission	1.51 (1.05-2.17)	0.024	1.55 (1.06-2.25)	<b>0.023</b>
Right ventricle HF symptoms	1.62 (1.13-2.32)	0.009	2.72 (1.15-6.40)	<b>0.019</b>
C-reactive protein ≥ 31.4 mg/l	1.97 (1.25-3.10)	0.004	2.75 (1.16-6.53)	<b>0.022</b>
Sodium ≤ 137 mmol/l	1.97 (1.27-3.06)	0.003	3.42 (1.32-8.87)	<b>0.011</b>
High-sensitivity troponin T ≥ 0.044 ng/ml	2.0 (1.39-2.90)	< 0.001	1.67 (1.12-2.50)	<b>0.012</b>
Creatinine ≥ 1.15 mg/dl	1.47 (1.03-2.12)	0.039	-	-
NT-proBNP ≥ 2453 ng/l	2.25 (1.47-3.45)	< 0.001	3.21 (1.12-5.87)	<b>0.004</b>
Infection at hospitalization	2.74 (1.59-4.73)	< 0.001	-	-
Amine therapy	3.17 (1.54-6.50)	0.002	1.59 (1.10-2.29)	<b>0.014</b>
Mechanical ventilation during hospitalization	2.19 (1.11-4.31)	0.024	3.85 (1.35-11.03)	<b>0.012</b>

Abbreviations: HR – hazard ratio; other: see Table 1

### Clinical characteristics and prognosis depending on age

Patients aged ≥ 65 years more frequently had a history of coronary artery disease (CAD) (72% vs. 45%,  $p < 0.001$ ), and higher rate of revascularization (47% vs. 26%,  $p = 0.004$ ); similarly, older patients more frequently had history of atrial fibrillation/flutter (39% vs. 24%,  $p = 0.040$ ). Older patients who required longer hospitalization (median 8 vs. 7 days,  $p = 0.035$ ) were characterized by lower hemoglobin and higher creatinine values and statistically significantly higher tro-

ponin levels (Table 4). It should be noted that the elderly group had a higher left ventricular ejection fraction (LVEF) and HF with LVEF > 40% was reported significantly more often (Table 4). Regarding the pharmacological treatment, the subgroup ≥ 65 years old was significantly less often treated with aldosterone antagonists (spironolactone and eplerenone) and more often with statins. Composite end-points were significantly more frequent in the elderly subgroup in comparison to younger: 65% vs 49% ( $p = 0.024$ ), including a trend towards higher all-cause mortality (38% and 24% respectively,  $p = 0.057$ ).

Table 4. Baseline clinical characteristics of the study patients in comparison between &lt; 65 and ≥ 65-year old patients

Parameters	Age < 65 n = 68	Age ≥ 65 n = 135	p
Male, n (%)	55 (81)	89 (66)	0.033
<b>Medical history</b>			
Coronary artery disease, n (%)	30 (45)	96 (72)	<b>&lt; 0.001</b>
Revascularization (PCI/CABG), n (%)	18 (26)	64 (47)	<b>0.004</b>
ICD (including CRT-D)	13 (19)	19 (14)	0.320
Atrial fibrillation/flutter, n (%)	16 (24)	52 (39)	<b>0.040</b>
Hypertension, n (%)	22 (32)	53 (39)	0.359
Diabetes mellitus, n (%)	13 (19)	33 (24)	0.478
Cancer, n (%)	2(9)	11(19)	0.331
<b>Cause of hospitalization</b>			
Infections, n (%)	23 (34)	51 (38)	0.644
Acute coronary syndrome, n (%)	1 (1)	7 (5)	0.272
Tachyarrhythmias, n (%)	15 (22)	35 (26)	0.607
Unknown reason, n (%)	34 (50)	44 (33)	<b>0.022</b>
Other, n (%)	3 (4)	18 (13)	0.053
The length of hospitalisation (days)	7 (4-9)	8 (5-12)	<b>0.035</b>
<b>Clinical and diagnostic parameters</b>			
Resting heart rate (beats /min)	90 (75-115)	83 (70-110)	0.136
SBP (mmHg)	115 (106-130)	124 (115-135)	<b>0.007</b>
NYHA class IV at admission, n (%)	32 (47)	50 (37)	0.225
Right ventricle HF symptoms at admission, n (%)	20 (29)	52 (39)	0.217
Hemoglobin (g/dl )	14.2 (12.4-15.6)	13.4 (11.7-14.7)	<b>0.041</b>
C-reactive protein (mg/l )	7.9 (4.7-15.7)	6.9 (3.4-20.3)	0.360
Sodium (mmol/l)	140 (138-141)	140 (138-142)	0.076

Glucose (mg/dl)	113 (98-143)	120 (102-154)	0.221
High-sensitivity troponin T (ng/ml)	0.028 (0.018-0.05)	0.034 (0.019-0.069)	0.064
Creatinine (mg/dl)	0.95 (0.8-1.3)	1.1 (0.9-1.5)	<b>0.005</b>
NT-proBNP (ng/l)	3418 (863-7384)	4416 (1809-8557)	<b>0.027</b>
<b>Echocardiographic parameters</b>			
LVEF (%)	30 (20-39)	38 (27-50)	<b>0.002</b>
LVEF < 40, n (%)	51 (75)	72 (54)	<b>0.013</b>
LVEF 40-49, n (%)	8 (12)	27 (20)	
LVEF ≥ 50, n (%)	9 (13)	35 (26)	
Diastolic dysfunction 2/3°, n (%)	40 (80)	71 (72)	0.274
Left atrium diameter (cm)	5 (4.5-5.3)	4.9 (4.5-5.3)	0.166
Right ventricular systolic pressure increased, n (%)	59 (91)	120 (91)	1.000
<b>In-hospital treatment</b>			
Amine, n (%)	6 (9)	3 (2)	0.063
Mechanical ventilation, n (%)	7 (10)	4 (3)	<b>0.045</b>
<b>Treatment at discharge</b>			
ACE-inhibitor/ Sartans, n (%)	55 (83)	113 (85)	0.836
Spirolactone /Eplerenone, n (%)	41 (63)	56 (43)	<b>0.015</b>
Beta-adrenolytics, n (%)	59 (91)	119 (92)	0.784
Statins, n (%)	36 (55)	94 (73)	<b>0.016</b>
Diuretics, n (%)	62 (95)	121 (94)	0.754
Potassium, n (%)	41 (63)	96 (74)	0.132
Antiplatelet therapy, n (%)	18 (28)	41 (32)	0.622
NOAC, VKA, LMWH, n (%)	41 (63)	96 (74)	0.132
Digoxin, n (%)	11 (17)	18 (14)	0.670
Amiodarone, n (%)	8 (12)	15 (12)	1.000



## Discussion

Our single-center retrospective study analyzed risk factors for poor prognosis in HF with particular attention to the elderly population. Over the years, many important risk factors for worsened HF prognosis have been reported, including clinical, laboratory and echocardiographic parameters [17-19]. Among the well-known clinical parameters: age, male sex, high NYHA class, low SBP, arrhythmias with rapid ventricular rate, infections, and the presence of comorbidities (e.g. ischemic heart disease, diabetes, renal failure, pulmonary disease, cancer) are the essential risk factors of poor prognosis [20-23]. The results of our study are congruent with this data: age  $\geq 73$  years old, SBP at discharge  $\leq 120$  mmHg, NYHA class IV at admission, symptoms of right ventricle HF, infection as the cause of initial hospitalization and concomitant diseases (cancer or atrial fibrillation/flutter) were significant predictors of composite end-points (all-cause mortality and rehospitalizations due to emergency reasons) in the two-year follow-up period. The hospitalization time was significantly longer for patients with the end-points in the observation period (Table 1), which is in agreement with the previous data from the literature [6]. Mechanical ventilation or catecholamine therapy, which according to our data was used more frequently in patients with the end-points, became significant risk factors for poor prognosis in both univariate and multivariate Cox analysis. Among the laboratory parameters, the most robust predictors according to the literature are renal function, hyponatremia, increased troponins, and low hemoglobin [18-19, 24-25]. Our results confirm this data (Table 3).

### The specific characteristics of the elderly population

It is well-known that elderly patients often present with complex comorbidities (hypertension, CAD, atrial fibrillation, peripheral vascular disease, kidney failure, or anemia) compared to the younger population [5, 26]. We confirmed this observation in our study (Table 4). Epidemiological data shows that CAD is the dominant comorbidity and the HF's main etiological unit [7]. In the presented project, almost 3 out of 4 patients from the elderly subgroup had CAD diagnosis. Additionally, these patients underwent revascularization more frequently, which is in agreement with the general trend observed in cardiology: the elderly may benefit more from invasive treatment, despite a higher periprocedural risk [27-28]. The general percentage of revascularized patients is surprisingly low in the study group with the diagnosis of CAD, although not every CAD patient requires invasive treatment. What is more, that could reflect the real condition of invasive treatment in a district hospital. The second most common comorbidity associated with HF, especially in the elderly, is

atrial fibrillation. Data from the literature and large registries (EORP-AF, Framingham Heart Study [29-30]) confirm the increased rate of this arrhythmia with the aging of the population and the occurrence of HF exacerbations in the elderly [29, 31-32]. We also observed this correlation in our study: the number of patients with a history of atrial fibrillation was almost twice as high in the subgroup  $\geq 65$  years old, compared to subgroup  $< 65$  years old: 39% vs. 24% ( $p = 0.040$ ). According to the literature, arterial hypertension is another comorbidity increasing the number of hospitalizations in the elderly [17, 20] and although in our study these differences were not statistically significant, its incidence was higher (Table 4).

In the senior population laboratory tests typically show deterioration of kidney function and anemia [20, 24], both of which were noted in our study (Table 4). Particular attention should be paid to the role of the assessment of natriuretic peptides in older patients hospitalized due to exacerbation of HF. It is known that NT-proBNP predicts mortality among the older and very elderly patients with chronic HF [33]. In the elderly population with HF, the higher cut-off value for NT-proBNP should be considered. In our study, it was 2453 ng/l for the composite end-points prediction (Table 2), while in the study by Vergaro et al. for the prognosis of the annual death of people aged  $\geq 77$  years old, it was as high as 4188 ng/l [34].

During the last twenty years, it was established that a significant percentage of patients with HF, especially the elderly, have preserved left ventricular systolic function [5, 21, 26, 35]. The latest HF guidelines published by the European Society of Cardiology [8] distinguish HF with LVEF that is significantly reduced ( $< 40\%$ ), moderately reduced (LVEF 40-49%) and preserved ( $\geq 50\%$ ). A fascinating result of the presented study is a statistically significant higher incidence of patients with LVEF of  $\geq 40\%$  in the subgroup of older adults. Moreover, the median LVEF value in these patients was also higher (Table 4). It is of note that the diameters of the left atrium did not differ statistically between the groups, which could explain that the enlargement of the left atrium is not only consequence of the diastolic but systolic dysfunction as well.

### Comparison of post-hospital recommendations according to the age

Data from the literature shows that older patients with HF are characterized by worse pharmacotherapy compared to younger patients [36]. This may be explained by numerous comorbidities and complications resulting from the use of certain groups of drugs or insufficient compliance [37]. The results of our single-center study present a therapy that can be considered optimal in comparison to the current guidelines [8, 38], because the percentage of people  $\geq 65$  years of age who use beta-blockers, ACE inhibitors/sartans remains high, which is consistent with the data from the Polish arm of the Heart Failure Pilot Survey

conducted in 26 Polish cardiological centers [12]. The exception is the percentage of patients using mineralocorticoid antagonists, which in the for the subgroup  $\geq 65$  years of age is 43%. This group is half the size of the subgroup of patients  $< 65$  years of age who were taking mineralocorticoid antagonists. It can be associated with a more frequent occurrence of comorbidities, including chronic renal disease which can be exacerbated by these medications. This trend of lower adherence to current guidelines in the geriatric population, resulting from poorer renal function, is also confirmed by data from the literature [28, 37]. There are encouraging reports of a slight improvement in prognosis in this challenging group of patients taking spironolactone at  $\text{GFR} > 30 \text{ ml/min/1.73m}^2$  [39], which may be an essential therapeutic direction in the future. Our results indicate an interesting trend towards greater use of anticoagulant and antiplatelet therapy in the elderly (Table 4), which is most likely due to both a higher proportion of CAD and atrial fibrillation in this subgroup. The above data is in agreement with the results from the European registers [29].

It should be noted that the percentage of patients enrolled in the study with implantable cardioverter-defibrillators (including cardiac resynchronization therapy) is disproportionately small concerning the number of patients with  $\text{LVEF} < 40\%$  and even lower in the elderly patients (Table 4). We precisely analyzed and discussed this problem in our previous study [15]. It also seems interesting that the subgroup with the composite end-points, was characterized by a higher rate of implanted ICD/CRT. This situation can be explained by the fact, that patients with implanted ICD and CRT devices usually have a worse prognosis. In addition, these devices protect mainly against life-threatening arrhythmic events and not against the other causes of cardiac death.

### **The prognosis of HF patients according to age**

The latest data from the literature suggests that the overall mortality in the senior population is decreasing: the age-standardized death rate has decreased by 40%, and the mean age of death due to HF has increased from 80.0 to 82.7 years in seven European countries during the last two decades [37]. The survival of HF patients is low, amounting to 17% in the first year after diagnosis and approximately 40–50% in 5 years, which is a worse result than in the case of many cancers [14]. Data from the literature on patients with HF in the geriatric population shows that their mortality is slightly over 20% within one year of diagnosis [12, 37], increasing to 36.7% after two years [37]. In our study, the 2-year mortality in patients  $\geq 65$  years old was similar and amounted to 38%, which confirms the above-mentioned European trend of improving mortality in the geriatric population. However, this percentage is still higher than in the younger population.

As we mentioned in the introduction, hospitalizations due to HF exacerbation are the leading cause of hospital admissions, particularly in patients  $> 65$  years old [5]. According to the ESC-HF Pilot registries, the general population's rehospitalization rates within one year amounted to 43.9% [14]. Korean studies conducted in patients  $> 65$  years hospitalized for HF within 30 days showed a 34.6% rehospitalization rate [40]. Even more alarming results are reported by Tuppin et al. [22], who collected information from the national health insurance information system about hospitalizations in France in 2009, where the 2-year all-cause readmission rate was 69%. In our 2-year observation, as many as 65% of seniors experienced death or rehospitalization due to emergency cases, which was significantly greater than in the younger subgroup. That results seem to confirm that more extensive studies based on the elderly population are needed.

### **Study limitations**

Our study has several limitations. First of all, it was a single-center, retrospective analysis and our results should thus be interpreted with caution. The study group is small and included only patients with HF exacerbation as the main diagnosis. In addition, some clinical data was not available in the documentation (e.g. the assessment of hypercholesterolemia, the width of the QRS complex, pre-admission drugs, smoking), hence the statistical evaluation of our data may raise some doubts.

### **Conclusions**

Simple clinical parameters (e.g. age, systolic blood pressure, NYHA class IV, right ventricle HF symptoms, increased natriuretic peptide, C-reactive protein, troponin, hyponatremia) as well as catecholamine therapy and mechanical ventilation during hospitalization due to HF exacerbation, are the substantial, independent risk factors for poor prognosis. The elderly patients are characterized by more comorbidities, worse laboratory results, higher HF frequency with moderately reduced LVEF and worse prognosis. Our pilot study could help in decision-making on the intensification of outpatient and inpatient treatment to increase its effectiveness. In turn, this could translate into a reduction of the frequent end-point events, a reduction in the frequency of hospitalizations, improved prognosis and measurable economic benefits.

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