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The prevalence and determinants of multimorbidity in hospitalized patients with heart failure

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Abstract: Objective: The aim of this study was to assess the prevalence of multimorbidity and co-existed diseases in hospitalized patients with heart failure (HF) in relation to age and gender.
Methods: The nationwide cross-sectional survey had been conducted in Poland (April-November 2013), in 260 randomly selected hospital wards. A trained nurse contacted with one physician, drawn from the list of all doctors working in the selected hospital's wards, who completed the study questionnaires regarding to clinical characteristics of the last five HF patients, who were discharged from an internal or cardiology ward.
Results: Mean age ± SD of the patients was 72.1 ± 10.1 years, 50% were female but the women were significantly older than men. Criterion of multimorbidity met almost 100% of the HF patients. There were no significant differences in the number of co-existed cardiovascular (CV) and non-CV diseases according to gender, but different clinical profile of HF men and women was observed. Women more frequently had thyroid disease, peripheral artery disease and cognitive impairment, whereas men was characterized by higher prevalence of cardiac, pulmonary and hepatic diseases. The co-morbidity significantly increased with age, notably due to increasing prevalence of non-CV diseases. Diabetes, chronic kidney disease, hypercholesterolemia and anemia were the most common non-CV diseases. Among HF patients, 83% suffered from three or more co-morbidities.
Conclusions: The study confirms, that multimorbidity is a considerable problem in patients with HF. Besides age, multimorbidity pattern is strongly dependent on gender. The multidisciplinary approach is warranted in particular in elderly subjects who suffer from HF.

Key words: heart failure, multimorbidity, co-morbidity, hospital settings, cross-sectional survey.

Introduction

Heart failure (HF) is a clinical syndrome characterized by high morbidity and mortality rates and it is an increasingly important public health problem — it is estimated that there is about 23 million patients worldwide with HF [1]. Prevalence of HF has increased with age up to 17.4% among subjects 85 years of age or older [2]. It has been estimated that in the Polish population 700-800 thousand people are currently suffering from HF [3, 4], and more than one in five people will experience HF at some point in their lives [5]. On the basis of data from the National Health Fund (NHF) in Poland in 2016 nearly 160 thousand hospitalizations related to HF occurred, of which about 10% ended in death [6]. In Europe, the observational Heart Failure Pilot Survey (ESC-HF Pilot) showed 12-month hospitalization rate of 44% among hospitalized patients with HF. Moreover, 12 month all-cause mortality rate was 17% and most deaths were due to cardiovascular (CV) causes [7].

Multimorbidity is defined as the co-occurrence of at least two chronic diseases or medical problems [8], and its related to disability, worsening of quality of life and higher health care costs [9]. In the studies which have been undertaken so far, the incidence of multimorbidity was shown to be disparate, due to the different populations included in the study, various settings and definition [10]. According to the American data, more than one quarter of adults have multimorbidity [11]. HF mostly is accompanied by co-existing illnesses which further aggravate the quality of life and prognosis, mainly because of the higher risk of adverse drugs reactions, great possibility of drugs interactions, conflicting medical advice, and unnecessary hospitalizations. The majority (74%) of outpatients with chronic HF in Europe have at least one co-morbidity [12]. Among the most common co-existing chronic diseases were chronic kidney disease (CKD), anemia, diabetes [12], chronic obstructive pulmonary disease (COPD), depression and lower respiratory diseases [13], and all of them were independently associated with increased risk of mortality and hospitalization. Moreover, it was shown that risk of hospital admission strongly raised with the number of coexisting chronic conditions [13]. Van Deursen *et al.* showed the association between the prevalence of co-morbidities and age, higher heart rate as well as ischaemic aetiology of HF and more severe signs of HF expressed by the New York Heart Association (NYHA) functional classification [12].

The aim of the study was to assess multimorbidity and co-existed chronic diseases in HF patients admitted to the hospital, independently of the cause of hospitalization. These issues were considered through the prism of the potential age and gender differences.

Materials and methods

Study design

The cross-sectional, nationwide, retrospective survey on HF management in hospital settings had been conducted in 2013 in Poland. The study methods have been published elsewhere [14]. In brief, the survey was carried out in 260 hospital wards randomly selected from the Registry of Entities Carrying out Medical Activities (Rejestr Podmiotów Wykonujących Działalność Leczniczą) — dated on April 2013. The method of stratified sampling was used for selection of the hospitals. The first stratum was one of the 16 voivodships, the second included regional, provincial, urban and university hospitals having internal wards, internal wards with cardiac beds and cardiology units. The trained nurses contacted physicians invited to the study and ask them to complete the study questionnaires concerning clinical characteristics of the patients and their management during the hospital stay. From the surveyed hospital ward one physician was asked to collect the data of the last five HF patients recently discharged from the hospital ward.

Patients' inclusion and exclusion criteria

The patients included to the survey had to have HF listed under the 'heading diagnosis' in the patient discharge card, however HF did not have to be the main cause of the surveyed hospitalization. The patient had to be discharged from the hospital ward in a stable health condition. A currently treated for oncologic condition was the only criterion excluding from the study.

Data collected

Data on patients' characteristics (gender, age), chronic diseases, past medical history on myocardial infarction (MI), stroke or transient ischemic attack (TIA), and major clinical conditions (hypercholesterolemia, cognitive impairment) were gathered up. Based on these data, the number of CV and non-CV diseases or clinical conditions was calculated, as well as the total number of concomitant diseases in HF patients was established. In addition, the selected results of the clinical assessment of the HF patients' status, such as a left ventricular ejection fraction (EF) extracted from the last echocardiography performed during the surveyed hospitalization and patients' NYHA class at their admission to the hospital ward were obtained.

Multimorbidity was assessed in the patients according to the most common definition as two or more chronic diseases or major medical conditions [8].

Ethical issues

Data were collected and processed maintaining confidentiality and anonymity of the surveyed patients and the physicians participating in the study. The study was approved by the Bioethics Committee of the Jagiellonian University (no. KBET/71/B/2011).

Statistical analysis

Continuous variables were summarized and presented as mean ± standard deviation (SD). Ordinal variables or variables not normally distributed were presented as median and quartile range (upper-lower quartile). Data on frequency were given as numbers and percentages. The comparative analyses were based on the Student's t-test or the Wilcoxon test, and the Chi-square test for qualitative data. The Cochrane-Armitage trend test or univariate analysis of variance were used to assess age-related changes, and Spearman correlation used to assess the relationship between number of co-morbidities and parameters of HF severity. Two-sided tests were used and the *P*-value was set at <0.05. Data were managed and analyzed using SAS v. 9.3 (SAS Institute Inc., Cary, NC, USA).

Results

Characteristic of the patients

Mean age (± SD) of the HF patients admitted to hospital was 72.1 ± 10.1 years, 26.3% of the patients were aged 80 years or above. In the study sample, proportions of women and men were equal, but women were significantly older (Table 1). At least two thirds of the patients had ischemic etiology of HF and majority of them were admitted to hospital due to the exacerbation of HF. Most of the studied population was classified on admission at NYHA III–IV class — more frequently women than men (Table 1). In the elderly and in women the higher left ventricular ejection fraction (LVEF) was observed. The elderly HF patients were more frequently hospitalized in internal wards, whereas the younger ones and men stayed more often in cardiology units.

Multimorbidity and comorbidity — gender and age differences

In fact, almost 100% of the surveyed HF patients were burdened multimorbidity, independently of gender (Table 2) and age (Table 3).

In men, cardiologic diseases were observed more frequently than in women (Table 2). Significantly more men suffered in the past from MI, as well as from valvular heart diseases, dilated cardiomyopathy and paroxysmal atrial fibrillation (AF). In women, the vascular diseases such peripheral artery disease (PAD) and hypertension were observed more frequently.

Table 1. Characteristic of the 1281 heart failure patients according to their age and gender.

	Gender			Age			
	Women n = 640	Men n = 641	*p*-value	≤59 yrs n = 144	60–79 yrs n = 800	≥80 yrs n = 337	*p*-value ǂ for trend
Age, years	75.2 ± 9.4	70.0 ± 9.8	<0.001	54.7 ± 4.3	70.4 ± 5.6	83.9 ± 3.6	<0.001
Female, n (%)	–	–		42 (29.2)	357 (44.6)	241 (71.5)	<0.001ǂ
HF as the main cause of hospitalization	489 (76.1)	468 (72.9)	0.195	105 (72.9)	604 (75.5)	244 (72.4)	0.502ǂ
HF cause≠							
ischemic (CHD/MI)	390 (60.8)	392 (61.0)	0.937	79 (54.9)	477 (59.6)	223 (66.2)	0.010ǂ
hypertension	136 (21.2)	156 (24.3)	0.188	33 (22.9)	187 (23.4)	72 (21.4)	0.576ǂ
arrhythmia	245 (38.3)	161 (25.0)	<0.001	25 (17.4)	265 (33.1)	116 (34.7)	0.002ǂ
valvular diseases	107 (16.7)	115 (17.9)	0.564	13 (9.0)	145 (18.1)	63 (18.7)	0.038ǂ
diabetes	119 (18.5)	95 (14.8)	0.070	18 (12.5)	132 (16.5)	64 (19.0)	0.083ǂ
inflammatory	40 (6.2)	22 (3.4)	0.019	8 (5.6)	36 (4.5)	18 (5.3)	0.885ǂ
toxic	9 (1.4)	29 (4.5)	0.001	14 (9.7)	23 (2.9)	1 (0.3)	<0.001ǂ
NYHA class at admission							
I–II	143 (22.3)	174 (27.4)	0.017	37 (25.9)	212 (26.7)	66 (19.7)	0.092
III	364 (56.8)	311 (48.9)		77 (53.8)	415 (52.2)	181 (54.0)	
IV	134 (20.9)	151 (23.7)		29 (20.3)	168 (21.1)	88 (26.3)	
LVEF							
number of available data (%)	528	474		113	650	236	
LVEF, %	45 [35–52]	35 [29–48]	<0.001	30 [25–46]	42 [30–50]	49 [38–55]	<0.001ǂ
Type of hospital ward							
internal	167 (58.2)	120 (41.8)	<0.001ǂ	23 (8.0)	140 (48.8)	124 (43.2)	<0.001
internal with cardiology beds	310 (53.6)	268 (46.4)		52 (9.0)	383 (66.3)	143 (24.7)	
cardiology	163 (39.2)	253 (60.8)		69 (16.6)	277 (66.6)	70 (16.8)	

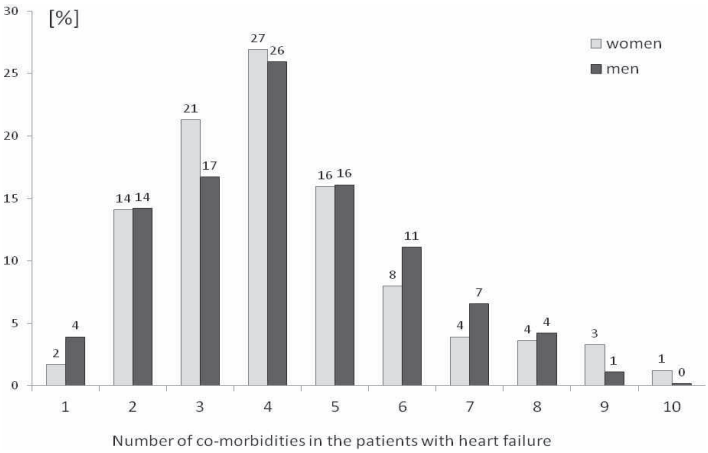
≠ based on the physician's knowledge or available data ǂ p-value for trend (the Cochrane-Armitage trend test).
Abbreviations: HF, heart failure; CHD, coronary heart disease; MI, myocardial infarction; NYHA, New York Heart Association; LVEF, left ventricular ejection fraction.
Data are presented as means ± standard deviation or median [upper-lower quartile].

Table 2. Multimorbidity and co-morbidity in HF patients admitted to the hospital according to the gender.

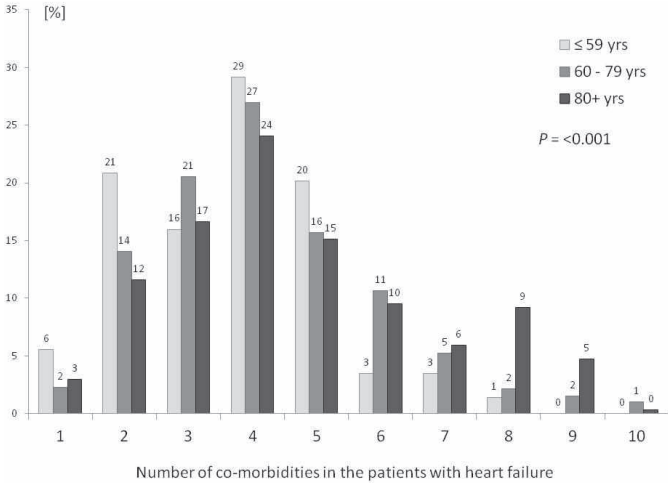
	Women n = 640	Men n = 641	*p*-value
Multimorbidity			
Two or more diseases, n (%)	639 (99.8)	633 (98.8)	0.038
CV co-existing diseases, n (%)			
Hypertension	527 (82.1)	494 (76.8)	0.062
Coronary heart disease	449 (70.2)	445 (69.4)	0.836
Myocardial infarction	185 (28.8)	243 (37.8)	0.003
Stroke or TIA	92 (14.3)	73 (11.4)	0.292
Valvular heart disease	162 (25.2)	197 (30.6)	0.031
Dilated cardiomyopathy	88 (13.7)	159 (24.7)	<0.001
Atrial fibrillation			
persisted	245 (38.2)	234 (36.7)	0.502
paroxysmal	117 (18.2)	131 (20.4)	0.046
Peripheral artery disease	189 (29.4)	127 (19.8)	<0.001
Abdominal aortic aneurysm ≥ 6 cm	1 (0.9)	13 (2.0)	0.403
Number of co-existing CV diseases	2 [2–3]	2 [2–3]	0.241
Non-CV co-morbidities, n (%)			
Diabetes	251 (39.1)	228 (35.5)	0.177
Hypercholesterolemia	191 (29.8)	242 (37.6)	0.003
COPD or asthma	99 (15.4)	128 (19.9)	0.041
Chronic kidney disease	229 (35.7)	203 (31.6)	0.120
Thyroid disease	127 (19.8)	88 (13.7)	0.009
Hepatitis or cirrhosis	16 (2.5)	30 (4.7)	0.036
Peptic ulcer disease	46 (7.2)	49 (7.6)	0.294
Connective tissue disease	6 (0.9)	8 (1.2)	0.851
Neoplastic disease	26 (4.1)	23 (3.6)	0.645
Tumor with metastasis	0 (0.0)	4 (0.6)	0.085
Anemia	151 (23.5)	141 (21.9)	0.496
Cognitive impairment	57 (8.9)	12 (1.9)	<0.001
Number of non-CV diseases	2 [1–3]	2 [1–3]	0.421
Total number of co-morbidities	4 [3–5]	4 [3–5]	0.624
≥3 co-morbidities, n (%)	538 (84.1)	524 (81.8)	0.299

Abbreviations: TIA, transient ischemic attack; CV, cardiovascular; COPD, chronic obstructive pulmonary disease. Data are presented as median [upper-lower quartile] or number (percentage).

There were no significant differences in the number of non-CV co-morbidities between men and women (Table 2), however the different clinical profiles of HF men and women have been found. In the surveyed HF men, pulmonary and liver diseases had been diagnosed more often, whereas in HF women — thyroid diseases. There were no significant gender-related differences in our HF patients with regard to prevalence of diabetes, CKD or anemia, however these co-morbidities were more common in HF women than in men. Distribution of the number of the co-morbidities in HF men and women presents the Fig. 1 (Panel A).



A



B

Fig. 1. Distribution of total co-morbidities according to the gender (Panel A) and age-category (Panel B).

Table 3. Multimorbidity and co-morbidity in HF patients admitted to the hospital in relation to the age-category.

	≤59 yrs n = 144	60–79 yrs n = 800	80+ yrs n = 337	*P*-value
Multimorbidity				
Two or more diseases, n (%)	144 (100.0)	791 (98.9)	337 (100.0)	0.445[‡]
CV co-existing diseases, n (%)				
Hypertension	103 (71.5)	660 (82.5)	256 (76.0)	0.001
Coronary heart disease	98 (68.1)	543 (68.1)	250 (74.6)	0.080
Myocardial infarction	46 (31.9)	281 (35.1)	99 (29.5)	0.057
Stroke or TIA	5 (3.5)	96 (12.1)	64 (19.0)	<0.001[‡]
Valvular heart disease	34 (23.6)	219 (27.4)	105 (31.2)	0.074[‡]
Dilated cardiomyopathy	55 (38.5)	161 (20.8)	28 (9.6)	<0.001[‡]
Atrial fibrillation				
persisted	24 (16.7)	303 (38.0)	150 (44.6)	<0.001[‡]
paroxysmal	29 (20.1)	160 (20.2)	57 (17.0)	0.292
Peripheral artery disease	19 (13.2)	188 (23.5)	109 (32.3)	<0.001[‡]
Abdominal aortic aneurysm ≥6 cm	1 (0.7)	16 (2.0)	3 (0.9)	0.109
Number of co-existing CV diseases	2 [2–3]	2 [2–3]	2 [2–3]	0.424
Non-CV co-morbidities, n (%)				
Diabetes	37 (25.7)	313 (39.1)	129 (38.3)	0.054[‡]
Hypercholesterolemia	53 (36.8)	278 (34.8)	99 (29.4)	<0.001
COPD or asthma	25 (17.4)	146 (18.3)	56 (16.6)	0.523
Chronic kidney disease	27 (18.8)	258 (32.2)	147 (43.6)	<0.001[‡]
Thyroid disease	16 (11.1)	130 (16.3)	66 (19.6)	0.016[‡]
Hepatitis or cirrhosis	12 (8.3)	32 (4.0)	2 (0.6)	<0.001[‡]
Peptic ulcer disease	11 (7.6)	53 (6.6)	31 (9.2)	0.587
Connective tissue disease	0 (0.0)	10 (1.2)	4 (1.2)	0.543
Neoplastic disease	2 (1.4)	29 (3.6)	18 (5.3)	0.036[‡]
Tumor with metastasis	3 (2.1)	1 (0.1)	0 (0.0)	0.032[‡]
Anemia	21 (14.6)	150 (18.8)	120 (35.6)	<0.001[‡]
Dementia	0 (0.0)	15 (1.9)	54 (16.0)	<0.001[‡]
Number of non-CV diseases	1 [1–2]	2 [1–2]	2 [1–3]	<0.001
Total number of co-morbidities	4 [2–5]	4 [3–5]	4 [3–6]	<0.001[‡]
≥3 co-morbidities, n (%)	106 (73.6)	668 (83.5)	288 (85.5)	0.006[‡]

Abbreviations: TIA, transient ischemic attack; CV, cardiovascular; COPD, chronic obstructive pulmonary disease. Data are presented as median [upper-lower quartile] or number (percentage).

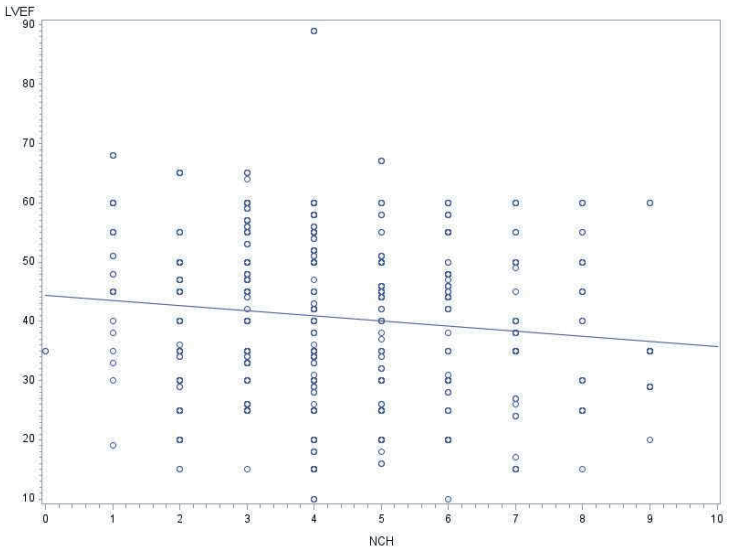
[‡] *p*-value for trend (the Cochrane-Armitage trend test).

With age, no significant increase of the number of CV diseases was observed (Table 3). However, MI and dilated cardiomyopathy had been recognized less frequently in the octogenarians than in the younger patients. Whereas, they suffered from stroke and transient ischemic attack (TIA), paroxysmal AF and PAD more frequently. Moreover, in the elderly HF patients non-CV co-morbidities had been observed more frequently (Table 3) — the most common were CKD, anemia, diabetes, thyroid diseases and cognitive impairments. In general, the percentage of the HF patients with co-occurence of additional three or more diseases was 83% (Table 3), and the number of co-morbidities significantly increased with age — Fig. 1 (panel B).

HF characteristics and co-morbidity

In the patients with severe HF (NYHA class IV), significantly more co-morbidities were observed than in those with NYHA class I–III, respectively: 4 [3–6] vs. 4 [3–5], $p = 0.009$. No significant differences between the patients staged with NYHA I–IV classes were observed in relation to the number of CV and non-CV diseases.

A significant inverse correlation was observed between the total number of co-morbidities and LVEF (Fig. 2). The further analysis showed the significant relationship only with regards to the number of CV co-morbidities and LVEF ($r = -0.172$, $p < 0.001$); the higher number of non-CV diseases was not associated with significant reduction of LVEF ($r = -0.009$, $p = 0.767$).



Legend: Spearman correlation $r = -0.116$, $p < 0.001$

Fig. 2. Association between left ventricular ejection fraction (LVEF) and the total number of co-morbidities (NCH).

Discussion

Summary of the results

In our study, multimorbidity criterion met almost all the HF patients. We found that those aged 60 years and older were hospitalized in internal medicine wards, whereas the younger ones in cardiology units more often. There was no statistical significance in the number of co-existed chronic diseases and clinical conditions according to the gender, however a different clinical profiles in HF men and women were observed. The total number of co-existed chronic diseases in HF patients significantly increased with age, mostly due to the increasing prevalence of non-CV comorbidities. The total number of the co-existed diseases was significantly related to the severity of HF symptoms expressed by the NYHA class and reduction of the LVEF, however the worsening of LVEF was not observed with increase number of the non-CV comorbidities.

Multimorbidity and co-morbidity

The systematic review of 41 studies has shown older age, female gender, and the lower level of education as the main risk factors for multimorbidity [9]. In our analysis, we showed that almost all examined HF patients were burdened with multimorbidity. Therefore, the further scope was placed on the analysis of HF as an index disease, with respect to the co-existing co-morbidities and its determinants.

Cardiovascular diseases, such as hypertension, coronary heart disease (CHD), arrhythmias were the most common concomitant diseases in our study, as well as in the previously published data [4, 15], as they remain etiologic factors for HF. With regard to the etiology of HF, our results were comparable to the results obtained in other studies which showed that the predominant cause of HF was ischemic heart disease [3, 16, 17].

In some cases, the cause of HF might be difficult to establish or may be multifactorial, not necessary only related to the CV diseases. In our study, among non-CV diseases, diabetes, CKD, hypercholesterolemia as well as anemia affected patients hospitalized with HF most frequently, and has been in line with some of the previous reports [4, 12]. However, some recently published results have shown a different data on the most frequent non-CV diseases accompanying HF, which may results from many reasons (study populations, regional conditions). The Italian study indicated that the most common co-morbidity in the HF patients admitted to hospitals in Italy was COPD [18]. The data from the European Heart Failure Pilot Survey showed that the patients from the Eastern Europe had less CKD and anemia, and the highest prevalence of diabetes, compared with the other European regions [12].

Our study highlighted the different clinical profiles of HF men and women, which was also observed in the other studies [19]. Additionally, the age- and gender-related differences has been found in the HF patients hospitalized at the internal and cardiology wards.

Moreover, in the presented study, similarly as in the previously published ones [12, 20], it has been shown that the number of concomitant diseases, especially the non-CV diseases, increased with advanced age of HF patient. This may suggest that in HF patients also non-CV co-morbidities might be responsible for the increased risk of re-hospitalization of older patients compared to the younger population of patients with HF.

Consequences of the co-existed diseases in HF

Edelmann's *et al.* study, which aimed to evaluate the relative impact of multiple co-morbidities on physical function using SF-36 physical functioning score (SF-36 PF score) and NYHA classification in HF patients, showed that almost all CV and non-CV co-morbidities, with exception of hypertension and obesity, were more frequent in HF patients with reduced EF (rEF). Most of the co-existed diseases had a negative effect on patients' general condition by increasing NYHA class and reducing SF-36 PF score, both in patients with rEF and with preserved EF (pEF). Obesity, CHD, PAD have been found to be especially unfavourable for patients with pEF. Interestingly, they found a much stronger impact of co-morbidities on NYHA class and physical impairment in patients with pEF than with rEF [21].

Moreover, in a study of Chamberlain's *et al.*, the patients with pEF had higher prevalence of chronic conditions with exception of osteoporosis, diabetes and cancer [22]. The observation seems particularly important given the fact that elderly patients and women are more likely to develop HF with pEF [23, 24]. In our study, we also found that older patients had higher LVEF which might suggest the potential relationship between the higher prevalence of non-CV diseases and the more frequently observed normal LVEF in this group.

In the study of Braunstein *et al.*, it was demonstrated that in the elderly HF population (>65 years old) risk of hospitalization was strongly increased with the higher number of chronic non-CV diseases [13]. Moreover, the study indicated that COPD, CKD, diabetes, depression and other lower respiratory diseases were associated with notably higher risk of hospitalizations and mortality. Similarly, in the study of Muzzarelli *et al.* it was indicated that most of readmissions were caused by the non-CV co-morbidities [25] such as anemia, renal failure, and depression. In Van Deursen's study it was found that the higher risk of mortality and hospitalizations in HF patients was independently associated with diagnosis of diabetes, CKD and anemia, as well as it was related to the number of co-morbidities [12]. The TEMISTOCLE

study has shown that HF patients with co-existing chronic diseases such as: COPD, CKD, anemia and/or thyroid disease, had longer stay in hospital, higher in-hospital mortality and also less often underwent non-invasive and invasive procedures compared to patients without these co-existed diseases [18].

The results of the previously published studies suggest that the chronic conditions, with other than HF pathophysiological pathways, might have a negative impact on outcomes of the patients with HF. This might be determined through the influence of polypharmacy, drug — drug, drug — diseases and disease — disease interactions, as well as difficulties in obtaining the optimal management and care coordination. A more comprehensive approach to diagnosis and treatment of patients with HF may improve the prognosis and the quality of life. The last European guidelines for the management of HF highlighted the problem of multimorbidity and presented a number of mechanisms by which co-existed diseases can adversely affect HF patients [26].

Strengths and limitations

The strength of the study is the nationwide coverage. This is probably the first Polish study on the large sample of hospitalized HF patients with analysis data on multimorbidity and specific co-existed chronic diseases.

However, the presented study should be interpreted in the context of some limitations.

First is the potential bias in selection of the patients reported by the physicians. In spite of our strong recommendations for the physicians, regarding to the selection of the patients to the survey, it cannot be ruled out that selection of the patients might have been based on the physicians' preferences in some cases.

The next important limitations are the retrospective study design and lack of external verification, both the diagnosis of HF as well as the other collected data.

Conclusions

Multimorbidity affects almost all patients with HF admitted to the hospital. We demonstrated different profile of co-existed chronic diseases according to age and gender. Therefore, the multidisciplinary approach is warranted in particular in elderly subjects who suffer from HF.

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Conflict of interest

None declared.

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