

Cardiovascular diseases and comorbidity in patients with chronic heart failure and preserved ejection fraction depending on age

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The aim of the study was to determine the cardiovascular diseases and comorbidity in patients with chronic heart failure and preserved ejection fraction depending on age. It was found that all patients with chronic heart failure with preserved ejection fraction have comorbid pathology. Revealed heterogeneity age changes in the comorbidity: prevalence of functional renal changes, chronic obstructive pulmonary disease, anemia increases with age. Moreover in all age groups, almost half of patients had obesity and a quarter of patients – diabetes mellitus type 2.

Key words: chronic heart failure, preserved ejection fraction, comorbidity, age.

Despite advances in modern medicine, heart failure is still the most common complication of many cardiovascular diseases and a major factor in mortality in the older age group [1, 3, 4, 6, 16, 19]. The growth rate of the chronic heart failure (CHF) occupies the first place among all cardiovascular diseases and the frequency of CHF increases with age [5, 9]. Recent studies of heart failure indicate a change in the patients composition depending on the left ventricular systolic function – increase in patients with heart failure and preserved left ventricle ejection fraction (LVEF) [5, 11, 12]. Increase of life expectancy in the world and population ageing, accumulation of cardiac and comorbid disease (anemia, endocrine diseases, diseases of the respiratory system, renal disease), increased mortality in the female population may be associated with an increase of CHF in particular with preserved ejection fraction [2, 9]. Modern methods of CHF treatments don't provide any decrease of mortality of patients with preserved ejection fraction, regardless of age and etiology of the disease [1]. Possibly patient survival depends not only on the etiology, but also on hemodynamic variant of CHF and comorbidity. It is possible that the role of the above mentioned mechanisms changes with age. In addition, there is no concrete protocol for diagnostics and treatment of heart failure with preserved ejection fraction [5, 15]. All of the above makes it necessary to look for possible factors in the development and progression of heart failure with preserved ejection fraction.

Literature review

Chronic heart failure (CHF) is a potentially fatal complication of any cardiovascular disease [1, 9]. Number of patients with chronic heart failure in the general population increases, which reduces the quality of life and rises the risk of adverse clinical results [4]. Unfortunately, modern treatment of heart failure is not yet able to influence the reduction of mortality of these patients to the population level [1, 4, 5, 9, 12].

Despite the presence of clinical signs of dysfunction, almost half of all patients have CHF with preserved LVEF [14]. More often CHF with preserved ejection fraction is present in the female population, in elderly patients with hypertension, anemia, obesity, chronic kidney disease, diabetes mellitus, chronic obstructive pulmonary disease [4]. It is proved

that the risk of death for patients with reduced LVEF is significantly higher compared to those with preserved LVEF, despite the fact that the progress of CHF has a poor prognosis [2]. It is also well known that among patients with CHF with reduced LVEF, patients with LVEF >35–40% have better prognosis for survival, as well as the patients who have LVEF >45% after treatment [8].

According to modern concepts, comorbid conditions seen as a direct cause of heart failure (hypertension, diabetes, obesity) [19]. Systemic inflammatory response reduces bioavailability of endogenous vasodilators and increases the activity of oxidative stress, which contributes to endothelial dysfunction and arterial endocardium. This artery endothelial dysfunction and endocardium consider essential for the development microvascular dysfunction of cardiomyocytes [1].

The approaches to the diagnosis and treatment of CHF with preserve EF are not developed and not approved [5, 10]. Resolving of this issue is very important because the point of this question depends on the choice of tactics and strategy of the CHF treatment. It is well-known that the development of cardiovascular disease, including CHF, has «classic» risk factors such as age, male gender, smoking, heredity, hypertension, obesity, diabetes and they play an important role [4]. However, about half the cardiovascular disease occur with none of modified most of these risk factors [16]. In connection with this important study factors determining peculiarities of heart failure in different age groups, the development of decompensation, the risk of adverse outcome in the end survival prognosis of patients in each case.

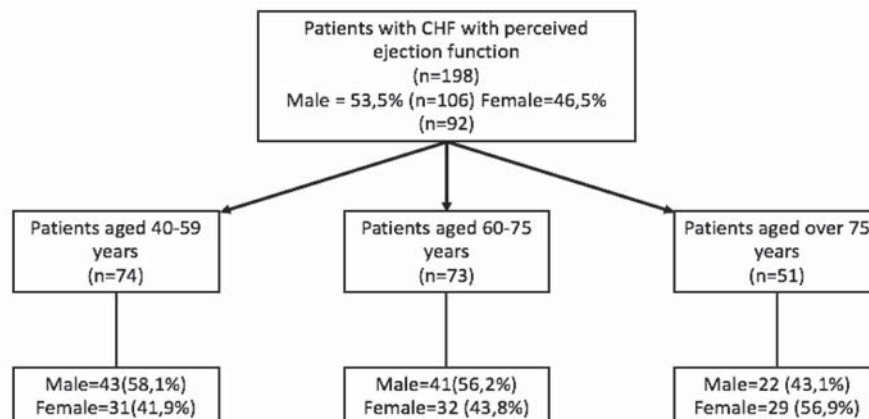
We can assume that survival of patients depends not only on the etiology, but also on hemodynamic option of CHF and comorbidity. With increasing life expectancy, comorbid diseases increase, and that possibly is a prevailing reason of the progression of heart failure [1]. The age certainly is significant in comorbidity, but how the way it affects key indicators is still not defined.

The aim was to determine the cardiovascular diseases and comorbidity in patients with chronic heart failure and preserved ejection fraction depending on age.

MATERIALS AND METHODS

A retrospective analysis of clinical records of 198 patients with CHF with preserved ejection fraction (EF more than 45%, average ($M \pm m$) – ($63,8 \pm 6,3\%$) was conducted. All patients were hospitalized in 2015 and were older than 40 years (average age ($M \pm m$) of $51,7 \pm 9,4$). 53,5% were males ($n=106$), 46,5% – females ($n=92$). With regard to the research and objectives, all patients were divided into three groups according to age: the first group – patients aged 40 to 59 years ($n=74$), the second group – patients aged 60 to 75 years ($n=73$), the third group – patients older than 75 years ($n=51$). The research design is shown in Fig. 2.1.

The inclusion criteria for patients in this research were: verified CHF; LVEF $\geq 45\%$.



The research design

Exclusion criteria: acute heart failure; CHF with ejection fraction less than 45%; myocardial infarction in anamnesis up to 6 months; stroke in the anamnesis up to 6 months; surgical heart intervention in history; acute renal injury.

CHF was diagnosed in case of presence of objective and subjective features inherent to this clinical syndrome, collected anamnesis, physical examination, laboratory and instrumental analysis (urinalysis, blood test, ECG, X-ray of the chest cavity, doppler-echocardiography, creatinine measurement, uric acid test). The diagnosis of CHF was set in the presence of clinical criteria, using the CHF Ukrainian Scientific Society of Cardiology classification, which was adopted in 2002 [5, 9]. Well-known clinical criteria of New York Heart Association (NYHA, 1964) were used to determine the functional class of patients [10].

The presence of hypertension (AH) and its stage were verified using classifications adopted in Ukraine and recommended for use in practice according to the Decree № 384 from 24.05.2012. To achieve the chosen aim, parameters were studied with the use of complying research protocol.

The method of body mass index evaluation. BMI was calculated using the standart formula [3].

Glomerular filtration rate (GFR) was calculated for the clinical evaluation of kidney function. The wide-spread formula,

derived during international multi-center study «Modification of Diet in Renal Disease Study (MDRD)» was used [13].

Concomitant kidney disease, thyroid cancer, obesity, diabetes, arrhythmias and conduction of the heart were determined in all patients.

Patients underwent ECG using an electrocardiograph in 12-lead: 6 – from the extremities (I, II, III, aVR, aVL, aVF), and 6 chest lead (V1-V6). ECG changes that indicate myocardial infarction were found among 52 patients (26,2%).

Indicators of intracardiac hemodynamics were assessed by echocardiographic examination on the unit «VIVID 3», GE Medical Systems in the left lateral position of patients. Measurements were carried out according to the recommendations of the American Society of echocardiography [5].

The methods of statistic analysis. Statistic processing of materials research conducted using the methods of biostatistics [6] implemented in the software package STATISTICA v.6.1 (Statsoft Inc., USA). Initial processing of the data was carried out by descriptive statistics with presentation of results for quantitative traits as: number of observations (n), the arithmetic mean (M), standard error of the mean value (m), median (Me); for qualitative attributes – in the form of ratios (intensive, extensive, indicators of visibility). The critical value of significance level (p) was taken ≤0,05.

Table 1

Predictors of CHF with preserved ejection fraction associated with cardiovascular diseases

Measure		Number of patients (abs., %) or middle level (M±m, Me)		
		Patients aged 40-59 (n=74)	Patients from 60 to 74 75 years (n=73)	Patients over 75 years (n=51)
Gender	Male	43 (58,1%)	41 (56,2%)	22 (43,1%)
	Female	31 (41,9%)	32 (43,8%)	29 (56,9%)
Stable angina pectoris	Absent	2 (2,8%)	17 (23,2%)	6 (11,8%)
	I-II FC	49 (66,2%)	28 (38,4%)	15 (29,4%)
	III FC	23 (31%)	28 (38,4%)	30 (58,8%)
Arterial hyper-tension	Absent	12 (16,2%)	17 (23,3%)	-
	II stage	43(58,1%)	39 (53,4%)	34 (66,7%)
	III stage	19 (25,7%)	17 (23,3%)	17 (33,3%)
Arterial hyper-tension	1 grade	4 (6,5%)	9 (12,3%)	2 (3,9%)
	2 grade	44 (71%)	39 (53,4%)	20 (39,2%)
	3 grade	14 (22,5%)	25 (34,3%)	29 (56,9%)
Myocardial infarction in anam-nesis		17 (23%)	23 (31,5%)	12 (23,5%)
CCD (blockades)		11 (14,9%)	5 (6,8%)	11 (21,6%)
Arrhythmia (extrasystole)		11 (14,9%)	15 (20,5%)	7 (13,7%)
Atrial fibrillation		6 (8,1%)	17 (23,2%)	7 (13,7%)

Presence of comorbid pathology among patients with CHF with preserved ejection fraction

Measure		Number of patients (abs., %) or middle level (M±m, Me)		
		Patients aged 40-59 (n=74)	Patients from 60 to 74 75 years (n=73)	Patients over 75 years (n=51)
COPD		2 (2,7%)	6 (10,2%)	4 (7,8%)
Renal disease		22 (29,7%)	19 (26%)	15 (29,4%)
Diabetes mellitus		18 (24,3%)	20 (27,4%)	10 (19,6%)
Thyroid gland disease		19 (25,7%)	28 (38,4%)	12 (23,5%)
BMI, kg/m ²	M±m (Me)	29,7±4,6	29,8± 4,0	26,8±3,0
BMI	Normal	23 (31%)	23 (31,5%)	15 (29,4%)
	Increased	18 (24,3%)	19 (26%)	13 (25,5%)
	Obesity	33 (44,6%)	31 (42,5%)	23 (45,1%)

RESULTS AND DISCUSSION

Various factors play a role in the development of CHF with preserved ejection fraction and its progression, according to the literature [5, 16]. Among them we can separate these groups. The first group of factors associated with the presence of cardiac disease: coronary heart disease (angina, postinfarction cardiosclerosis), hypertension, arrhythmias (extrasystoles, atrial fibrillation) and conduction (blockade). The second group – extracardiac factors: thyroid disease, chronic obstructive pulmonary disease (COPD), chronic kidney disease, obesity, diabetes, anemia. Cardiovascular diseases and extracardiac factors associated with CHF with preserved ejection fraction of patients from different age groups were analyzed.

Patients of all age groups were comparable in anamnesis and clinical characteristics ($p>0,05$). Women in the age group over 75 years – 29 (56,9%) prevailed among all other patients with CHF with preserved ejection fraction that matches with the data of worldwide studies about prevalence of women in the structure of CHF with preserved ejection fraction [3, 4, 15, 19].

Angina pectoris II and III functional class (FC) was diagnosed among 173 patients (87,3%) of all ages: FC II – among 49 (66,2%), FC III – 23 (31%) among patients up to 59 years old; among patients from 60 to 75 years: FC II among 28 (38,4%), FC III – 28 (38,4%) and patients older than 76: FC II among 15 (29,4%) and III FC among 30 (58,8%).

Hypertension was diagnosed among 169 patients (85,4%). From the first group 43 (58,1%) patients had stage II, 19 (25,7%) – III stage; in the second group, 39 (53,4%) patients – II stage, 17 (23,3%) – III stage; the third group, 34 (66,7%) – II stage, grade 1, 17 (33,3%) – the III stage. In III group all patients had hypertension (tab. 1).

17 (23%) patients from the first group had a myocardial infarction in anamnesis (over six months), 23 (31,5%) – in the second group and 12 (23,5%) – in the third group. Conduction (block) were in 11 (14,9%) patients from the first group, in 5 (6,8%) – from the second group and in 11 (21,6%) from the third group. Extrasystole was in 11 (14,9%) patients from the first group, in 15 (20,5%) from the second group and in 7 (13,7%) from the third group. Atrial fibrillation was detected in 6 patients (8,1%) from the first group, in 17 (23,2%) from second group, in 7 (13,7%) from the third group. Level of indicators such as myocardial infarction history, extrasystole, atrial fibrillation increases with age, but the highest in the age 60–75 years.

Comorbid diseases in patients with chronic heart failure with preserved ejection fraction, depending on age

We have studied through several factors that may induce CHF with preserved ejection fraction associated with extracardiac pathology: the presence of renal disease, thyroid cancer, obesity, diabetes, COPD (tab. 2).

During the analyzing the presence of comorbidity in patients

with heart failure with preserved ejection fraction found a high degree of comorbidity.

It was found that the frequency of registration of COPD increases with age: in the second age group the frequency of COPD is 7,5% higher than in the first, in the third – 4,1% higher. More than quarter of all patients had diabetes, which is consistent with results from UNIVERS [6]. Thyroid pathology was the highest in the group from 60 to 75 years. The average level of BMI in all groups were not significantly different and was responsible overweight. This found that in all groups registered a high incidence of obesity – almost half of the patients had obesity: in first group 33 (44,6%) patients, in second – 31 (42,5%) and 23 (45,1%) patients in third group (tab. 2).

Special analysis requires renal function in patients with CHF. According to the study, renal pathology (the presence of diabetic or hypertensive nephropathy, glomerulonephritis or pyelonephritis a history of kidney cysts) was found almost at third of patients of all ages. Also we have noticed that GFR was reduced in more patients.

Among them GFR below 60 ml/min/1,73 m² corresponding to chronic renal failure was found in 15 (20,2%) patients from the first group, 27 (37%) patients – from the second group and 29 (56,9%) from the third group.

Today, the presence of concomitant anemia in patients with CHF is a factor of negative clinical prognosis that in addition significantly reduces the quality of life of patients [2]. During analyzing the average levels of hemoglobin in all age groups found that the frequency of registration of low hemoglobin level was the lowest in the group till 59 years (16,3%). 14,9% of them were patients with medium level of anemia.

The presence of thyroid disease in patients with CHF (hypothyroidism, hyperthyroidism) verified under the Order of the MOH Ukraine № 507 from 28.12.2002 [6]. Established that the frequency of thyroid diseases registration increases with patients age. Most thyroid pathology was observed in the group of 60–75 years. Found that significant number among patients with CHF with preserved EF was in a hypothyroidism condition, and the number of patients also increased with age: from 5,4% in patients aged 40 to 59 to 12% in patients aged ≥75 years.

CONCLUSIONS

1. Increase in the occurrence of hypertension and prevalence of angina pectoris observed in the presence of CHF and with age growth. On the other hand, the highest degree of myocardial infarction and atrial fibrillation was found in the range of 60–75 years.

2. All patients with CHF with preserved ejection fraction have comorbid pathology. Revealed heterogeneity age changes in the comorbidity: prevalence of functional renal changes, chronic obstructive pulmonary disease, anemia increases with age. Moreover in all age groups, almost half of patients had obesity and a quarter of patients – diabetes mellitus type 2.

Серцево-судинні захворювання та коморбідність у пацієнтів з хронічною серцевою недостатністю зі збереженою фракцією викиду залежно від віку
Ю.С. Кушнір, О.В. Курята, Г.О. Доброгорська

Метою дослідження було встановити наявність серцево-судинних захворювань та коморбідність у пацієнтів з хронічною серцевою недостатністю зі збереженою фракцією викиду залежно від віку. У всіх пацієнтів з хронічною серцевою недостатністю зі збереженою фракцією викиду зустрічається супутня патологія. Виявлено гетерогенність вікових змін коморбідної патології: поширеність функціональних змін нирок, хронічні обструктивні захворювання нирок, анемії з віком зростає. До того ж, в усіх вікових групах майже половина пацієнтів мали ожиріння, а чверть пацієнтів – цукровий діабет 2-го типу.

Ключові слова: хронічна серцева недостатність, збережена фракція викиду, коморбідність, вік.

Сердечно-сосудистые заболевания и коморбидность у пациентов с хронической сердечной недостаточностью и сохраненной фракцией выброса в зависимости от возраста
Ю.С. Кушнир, А.В. Курята, Г.А. Доброгорская

Целью исследования было определить наличие сердечно-сосудистых заболеваний и коморбидность у пациентов с хронической сердечной недостаточностью и сохраненной фракцией выброса в зависимости от возраста. У всех пациентов с хронической сердечной недостаточностью с сохраненной фракцией выброса встречается сопутствующая патология. Выявлена гетерогенность возрастных изменений коморбидной патологии: распространенность функциональных изменений почек, хронические обструктивные заболевания легких, анемии с возрастом увеличиваются. Более того, во всех возрастных группах почти половина пациентов имели ожирение, а четверть пациентов – сахарный диабет 2-го типа.

Ключевые слова: хроническая сердечная недостаточность, сохраненная фракция выброса, коморбидность, возраст.

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