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Chronic Heart Failure in Patients Hospitalized in 2002 and 2021: Comparative Analysis of Prevalence, Clinical Course and Drug Therapy

Aim	Comparative analysis of the prevalence of chronic heart failure (CHF), clinical and medical history data, and drug therapy of patients admitted to a cardiology hospital in 2002 and 2021.
Material and methods	The study analyzed the medical records of patients with a confirmed diagnosis of CHF who were admitted in 2002 (n=210) and 2021 (n=381) to a specialized cardiology hospital.
Results	According to medical records of 2021, the proportion of patients with a confirmed diagnosis of CHF (87.6%) in the cohort of patients admitted to a cardiology hospital was twice as high as in 2002 (46.4%; p<0.001). The majority of patients with CHF in the study sample were patients with preserved left ventricular ejection fraction (HFpEF). The proportion of such patients significantly increased to reach 75.9% in 2021 compared to 58.6% in 2002 (p<0.001). At the same time, the number of severe forms of CHF (NYHA functional class (FC) IV) decreased by 10% and was 13.2% in 2002 and 1.3% in 2021 (p<0.001). In the majority of patients, ischemic heart disease (98.1 and 91.1% in 2002 and 2021, respectively, p<0.001) and hypertension (80.5 and 98.2%, respectively, p<0.001) were diagnosed as the cause for CHF. Furthermore, the incidence of comorbidity increased significantly: atrial fibrillation was detected in 12.3% of patients in 2002 and 26.4% in 2021 (p<0.001); type 2 diabetes mellitus, in 14.3 and 32% of patients (p <0.001); and obesity, in 33.3 and 43.7% of patients, respectively (p=0.018). The frequency of using the major groups of drugs increased during the analyzed period: renin-angiotensin-aldosterone system blockers were administered to 71.9% of patients in 2002 and to 87.7% in 2021 (p<0.001); beta-blockers were administered to 53.3 and 82.4% of patients (p<0.001); and mineralocorticoid receptor antagonists, to 1.9 and 18.6% of patients, respectively (p=0.004).
Conclusion	In 2021, the proportion of patients with a confirmed diagnosis of CHF in the patient cohort admitted to a cardiology hospital was twice as high as in 2002; the phenotype with preserved left ventricular ejection fraction predominated in the CHF structure. During the analyzed twenty-year period, the prevalence of comorbidities increased among CHF patients. The prescription frequency of pathogenetic evidence-based therapy has significantly increased by 2021, however, it remains insufficient even in patients with CHF with reduced left ventricular ejection fraction.

Keywords	Chronic heart failure; CHF; HFrEF; HFmrEF; HFpEF
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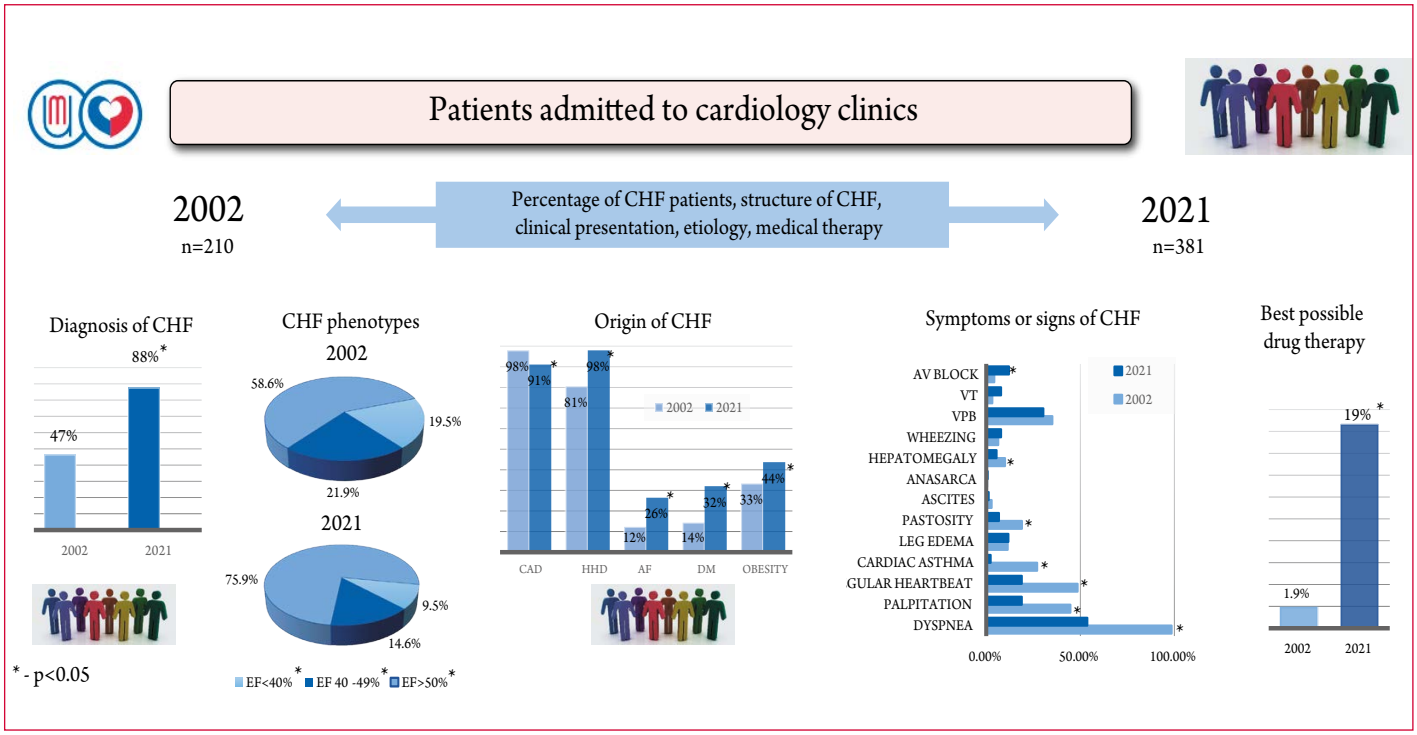
Introduction

Chronic heart failure (CHF) is one of the major concerns of clinical cardiology and healthcare, as the total number of patients with CHF is increasing continuously according to epidemiological studies, which is associated with increased survival rates and improved prognosis for patients with acute cardiovascular disease (CVD), on the one hand, and with the worsening comorbid background of cardiac patients, on the other hand, due to population growth

Central illustration. Chronic Heart Failure in Patients Hospitalized in 2002 and 2021: Comparative Analysis of Prevalence, Clinical Course and Drug Therapy



and global aging. According to global statistics, approximately 64 million people worldwide have CVD, and more than 1 million new cases are diagnosed each year [1]. The total cost of care exceeds $40 billion annually. More than half of these costs are spent on hospital stays. It should be noted that mortality from CHF remains high, reaching 25% within 12 months of hospitalization for decompensated CHF. At the same time, mortality rates in heart failure with preserved ejection fraction (HFpEF) and heart failure with reduced ejection fraction (HFrEF) are not significantly different [2].

The prevalence of CHF is 1–2% among adults in Western countries. Rates are even higher, up to 6%, in some Asian countries. However, the true prevalence is likely to be higher because studies typically include only documented cases of CHF [3, 4]. The incidence of CHF increases with age, from 1% in those younger than 55 years to more than 10% in patients 70 years and older.

According to Russian epidemiological studies, the prevalence of CVD in the general population is 7–8% based on the criteria for CVD proposed in the EPOCH-CHF study [5]. For example, the prevalence of CHF was 8.2% according to the EPOCH-CHF study [6] and 7.9% according to the ESSE-RF study [7]. The issue of the prevalence of CHF in hospitalized patients with CVD deserves special attention and was the subject of the EPOCH-O-CHF study conducted in Russia in 2002 [8]. At the same time, modern studies assessing the prevalence of CHF in a cohort of hospitalized patients, analyzing the characteristics of its clinical course and prescribed drug therapy are currently insufficient.

Therefore, the objective of this study was to compare the prevalence of CHF, clinical and anamnestic characteristics, and drug therapy of patients admitted to cardiology clinics in 2002 and 2021.

Material and methods

A retrospective study was conducted, and 887 patients were included in the data analysis. The study protocol was performed in compliance with the Declaration of Helsinki and was approved by the local ethics committee (Minutes No. 207 dated 23/12/2020). We analyzed the medical records of patients admitted to two large departments of the Research Institute of Cardiology of Tomsk National Research Medical Center in the period from 01/01/2021 to 31/03/2021 (n=435); the comparison group consisted of patients included in the EPOCH-O-CHF study from similar departments of the Research Institute of Cardiology from 01/01/2002 to 31/03/2002 (n=452) [9]. In 2002, CHF was diagnosed by researchers according to the OSSN criteria (presence of dyspnea combined with echocardiographic evidence of cardiac damage or the need to prescribe diuretics) and/or the Framingham

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criteria (when two major criteria or one major and two minor criteria were combined) [8]. In 2021, CHF was diagnosed by an attending physician based on existing clinical guidelines [10], with natriuretic peptide levels measured in a limited number of cases in routine clinical practice. To confirm the diagnosis of CHF, all patients underwent echocardiography with assessment of left ventricular ejection fraction (LVEF) (Simpson's method), other echocardiographic criteria of structural heart changes (left ventricular hypertrophy and/or left atrial enlargement), and diastolic function. Diastolic function was assessed in all patients by estimating the ratio of the early to late early diastolic LV filling velocity (E/A) and the ratio of the mean early diastolic LV filling velocity to the mean lateral-medial mitral annular velocity (E/e').

Statistical analysis of the data obtained was performed using Statistica 10.0. The distribution of quantitative data was tested using the Shapiro-Wilk test. Quantitative data are expressed as the medians and interquartile ranges (Me [Q25; Q75]). Since the distribution of the quantitative data was non-normal, they were compared in two independent samples using the Mann–Whitney (U) test. Qualitative data are presented as absolute and relative values, and the significance of differences between them was assessed using the chi-squared test (χ^2) and two-tailed Fisher's exact test. The significance threshold for testing statistical hypotheses was set at 0.05.

Results

In 2002, CHF was verified in 46.5% of the total cohort of patients hospitalized in cardiac clinics (Group 1, n=210), whereas in 2021, 87.6% were diagnosed with CHF (Group 2, n=381; p<0.001). Males still prevail among patients with CHF (65.4%), and their age increased by a mean of 6 years during the period analyzed, as did the age of females (p<0.001 and p=0.031, respectively). Analysis of the sex and age distribution of patients showed that the number of females aged 60–69 years more than doubled (p=0.003), whereas the number of older females (70–79 years) decreased by 16%. The majority of male patients hospitalized were 60 years of age and older, with a significant increase in the number of male patients 80 years of age and older (Table 1).

Given the complex epidemiological situation in 2021, it should be noted that among the hospitalized patients of the analyzed group, 10% of patients (n=38) suffered COVID-19, almost a third of them were diagnosed with pneumonia requiring hospitalization. Of all patients with a history of COVID-19, 71% were male. All had coronary artery disease (CAD), hypertensive heart disease (HDD), one third had a history of myocardial infarction (MI), 8 patients had type 2 diabetes mellitus (DM), and 11 were obese.

CAD and HHD were the most common causes of CHF in 2021, as they were 20 years ago. Meanwhile, the number of patients with HHD increased from 80.5% to 98.2% (p<0.001), while the number of patients with CAD was 91.1% – 7% lower than in 2002. It should be noted that in the study cohort, the number of patients with a history of surgery for CAD (coronary artery bypass grafting, mammary artery bypass grafting) decreased significantly compared to 2002, while the number of endovascular procedures remained at the same level, which may be due to a decrease in the percentage of patients with CAD among those with CHF hospitalized in cardiac clinics. The incidence of comorbidities such as atrial fibrillation (AF) and diabetes mellitus (DM) more than doubled (p<0.001), and the number of patients with obesity increased by more than 10% (p=0.018) during the analyzed period. The percentage of patients experiencing a cerebrovascular accident (CVA) remained unchanged at 9.8% (p=0.942). Table 2 provides comparative characteristics of the patient groups.

The structure of CHF in terms of left ventricular ejection fraction (LVEF) changed significantly. At

Table 1. Distribution of patients with CHF admitted to cardiology clinics, according to sex and age

Age	Both male and female			Male			Female		
	2002 (n=210)	2021 (n=381)	p	2002 (n=147)	2021 (n=249)	p	2002 (n=63)	2021 (n=132)	p
Under 60	96 (45.7)	107 (28.1)	< 0.001	83 (56.5)	86 (34.5)	< 0.001	13 (20.7)	21 (15.9)	0.416
≥ 60	114 (54.3)	274 (71.9)	< 0.001	64 (43.5)	163 (65.5)	< 0.001	50 (79.3)	111 (84.1)	0.416
60–69	54 (25.7)	151 (39.6)	< 0.001	47 (31.9)	102 (40.9)	0.075	10 (15.9)	49 (37.1)	0.003
70–79	48 (22.9)	86 (22.6)	0.937	16 (10.9)	45 (18.2)	0.056	30 (47.5)	41 (31.1)	0.025
≥80	12 (5.7)	37 (9.7)	0.092	1 (0.7)	16 (6.4)	0.014	10 (15.9)	21 (15.9)	0.995

p is the significance of differences between the groups.

Table 2. Clinical characteristics of CHF patients

Parameter	Group 1 – 2002 (n=210)	Group 2 – 2021 (n=381)	p
Age, years, Me (Q25; Q75)	60 (52; 71)	65 (58; 71)	< 0.001
Male/female, n (%)	147 (70.1)/63 (29.9)	249 (65.4)/132 (34.6)	0.251
Age, years, male/female, Me (Q25; Q75)	60 (55; 66)/66 (58.3; 74)	63 (57; 69)/69 (62.3; 74)	<0.001/0.031
CAD, n (%)	206 (98.1)	346 (91.1)	< 0.001
History of coronary artery stenting, n (%)	52 (24.8)	95 (24.9)	0.963
History of CABG/ MCABG, n (%)	39 (18.6)	26 (6.8)	< 0.001
History of MI, n (%)	83 (39.5)	138 (36.3)	0.388
HHD, n (%)	169 (80.5)	374 (98.2)	< 0.001
DM type 2, n (%)	30 (14.3)	122 (32)	< 0.001
History of CVA, n (%)	20 (9.5)	37 (9.8)	0.942
AF, n (%)	26 (12.3)	100 (26.4)	< 0.001
Obesity, n (%)	70 (33.3)	165 (43.7)	0.018

CAD, coronary artery disease; CABG, coronary artery bypass grafting; MCABG, mammary coronary artery bypass grafting; MI, myocardial infarction; HHD, hypertensive heart disease; DM, diabetes mellitus; CVA, cerebrovascular accident; AF, atrial fibrillation; p is the significance of differences between the groups.

the same time, the majority of patients (76%) in 2021 were those with preserved LVEF, the number of which significantly increased (p<0.001), while the number of patients with mid-range and low LVEF significantly decreased (p=0.027 and p<0.001, respectively, Figure 1).

In 2021, the majority of patients still had NYHA (New York Heart Association) class II CHF, while the number of patients with high grade CHF decreased sharply. Given this, it was natural to expect the number of patients with milder clinical manifestations of CHF to increase. In fact, the portrait of a CHF patient has changed over the past twenty years: clinically severe forms of CHF with marked congestion, such as ascites, anasarca, hepatomegaly, cardiac asthma, have become less common. At the same time, the frequency of detection of rhythm and conduction disorders such as AF and atrioventricular (AV) block has increased. Table 3 shows the frequency of reporting symptoms and signs of CHF.

The analysis of drug therapy revealed a higher use of major classes of drugs such as renin-angiotensin-aldosterone system (RAAS) inhibitors and mineralocorticoid receptor antagonists. Sacubitril-valsartan was

Table 3. Symptoms and signs of CHF in patient groups

Parameter	Group 1 – 2002 (n=210)	Group 2 – 2021 (n=381)	p
CHF class I, n (%)	52 (24.8)	94 (24.7)	0.981
CHF class II, n (%)	80 (38.1)	192 (50.4)	0.005
CHF class III, n (%)	49 (23.3)	90 (23.6)	0.937
CHF class IV, n (%)	29 (13.2)	5 (1.3)	< 0.001
Dyspnea, n (%)	207 (98.6)	204 (53.8)	< 0.001
Palpitation, n (%)	94 (44.8)	72 (18.9)	< 0.001
Irregular heartbeat, n (%)	102 (48.6)	72 (18.9)	< 0.001
Cardiac asthma, n (%)	57 (27.1)	9 (2.4)	< 0.001
Leg edema, n (%)	24 (11.4)	45 (11.8)	0.89
Pastosity, n (%)	40 (19)	26 (6.8)	< 0.001
Ascites, n (%)	6 (2.9)	5 (1.3)	0.184
Anasarca, n (%)	1 (0.5)	3 (0.8)	0.6
Hepatomegaly, n (%)	21 (10)	21 (5.5)	0.043
Wheezing, n (%)	24 (6.4)	30 (7.9)	0.152
VPB, n (%)	75 (35.2)	116 (30.4)	0.19
VT, n (%)	7 (3.3)	30 (7.9)	0.457
AV block, n (%)	9 (4.3)	46 (12.1)	0.004
Need for pacemaker implantation due to cardiac conduction disturbance during hospital stay, n (%)	Not available	2.9 %	–
Dyspnea and/or any signs of congestion and/or need for loop diuretics, n (%)	207 (98.6)	245 (64.3)	< 0.001

CHF, chronic heart failure; AF, atrial fibrillation; VPB, ventricular premature beat; VT, ventricular tachycardia; AV, atrioventricular; p is the significance of differences between the groups.

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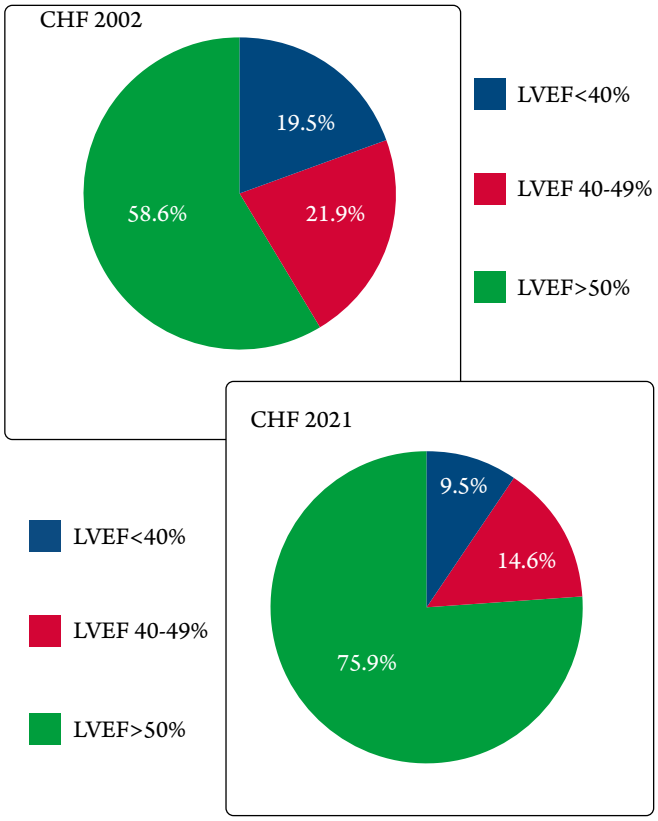
Figure 1. Prevalence of heart failure types among patients admitted to cardiology clinics



also prescribed to some patients in 2021 (1.3%). There was an increase in the frequency of anticoagulant use, which is a natural consequence of higher incidence of AF. It is necessary to mention positive changes in terms of lipid metabolism correction – the overwhelming majority of patients (94%) received hypolipidemic therapy with statins (Table 4).

Drug therapy was analyzed in groups according to LVEF. RAAS blocker therapy and triple neurohormonal blockade in general were used more frequently in all groups. It should be noted that 13.9% of patients with HFrEF received sacubitril-valsartan; the frequency of administration of RAAS inhibitors did not change. Angiotensin-converting enzyme (ACE) inhibitors and beta-blockers (BBs) were prescribed more frequently in patients with heart failure with mid-range ejection fraction (HFmrEF). Interestingly, the frequency of administration of mineralocorticoid receptor antagonists (MRAs) increased 1.5–2 times in the HFpEF group.

Discussion

The analysis showed that the percentage of patients with a documented diagnosis of CHF in the cohort of patients hospitalized in cardiology clinics doubled over two decades. The mean age of patients in this category increased by 6 years. At the same time, it should be noted that the majority of men admitted to the hospital were over 60 years of age; moreover, the number of male patients over 80 years of age increased significantly, confirming epidemiological data on increasing life expectancy and the global aging of the population.

Regarding the clinical picture of CHF, it is noteworthy that severe forms of CHF with pronounced congestion and significant limitation of physical activity and quality of life were significantly less frequent in 2021 (1.3% of cases) compared to 2002 (13.2% of cases; p<0.001). At the same time, the majority of hospitalized patients with documented CHF were patients with HFrEF, which is consistent with the results of most Russian studies [11, 12]. In studies conducted in Europe and the United States, the number of patients with HFrEF is approximately

Table 4. Medical therapy for patients with CHF prescribed at the time of discharge from cardiology clinics

Parameter	Group 1 – 2002 (n=210)	Group 2 – 2021 (n=381)	p
ACE inhibitors, n (%)	139 (66.2)	272 (71.4)	0.189
ARBs, n (%)	12 (5.7)	60 (15.7)	< 0.001
Sacubitril-valsartan, n (%)	0	5 (1.3)	0.1
RAAS blocker, n (%)	151 (71.9)	334 (87.7)	< 0.001
BB, n (%)	112 (53.3)	314 (82.4)	< 0.001
Any MRA, n (%)	7 (3.3)	93 (24.4)	0.004
Eplerenone, n (%)	0	27 (7.1)	< 0.001
Diuretics, n (%)	107 (51)	185 (48.6)	0.578
Cardiac glycosides, n (%)	35 (16.7)	10 (2.6)	< 0.001
Antiplatelet drugs, n (%)	180 (85.7)	297 (78)	0.023
Anticoagulants, n (%)	51 (24.3)	126 (33.1)	0.026
Statins, n (%)	15 (7.1)	358 (94)	< 0.001
Calcium channel blockers, n (%)	34 (16.2)	150 (39.4)	< 0.001
Triple neurohormonal blockade, n (%)*	4 (1.9)	71 (18.6)	< 0.001

ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blocker; RAAS, renin-angiotensin-aldosterone system; BB, beta-blocker; MRA, mineralocorticoid receptor antagonist; *RAAS blocker (ACE inhibitor or ARB) + BB + MRA; p is the significance of differences between the groups.

Table 5. Frequency of prescribing the main groups of drugs in patients with CHF with different levels of LVEF

Drug group	LVEF<40 %			LVEF 40–49 %			LVEF > 50 %		
	2002 (n=41)	2021 (n=36)	p1	2002 (n=46)	2021 (n=56)	p2	2002 (n=123)	2021 (n=289)	p3
ACE inhibitors, n (%)	32 (78)	26 (72.2)	0.744	29 (63)	49 (89.1)	0.002	78 (63)	194 (67.8)	0.386
ARBs, n (%)	1 (2.4)	2 (5.5)	0.5	4 (8.7)	4 (7.3)	> 0.05	7 (5.7)	53 (18.5)	< 0.001
Sacubitril-valsartan, n (%)	0	5 (13.9)	0.02	0	0	–	0	0	–
RAAS blocker, n (%)	33 (80.4)	32 (88.9)	0.485	33 (72)	52 (94.5)	0.005	85 (69)	246 (86)	< 0.001
BB, n (%)	27 (68)	30 (83.3)	0.138	25 (54)	51 (92.7)	< 0.001	60 (49)	229 (80.1)	< 0.001
MRAs, n (%)	4 (9.7)	29 (80.6)	< 0.001	2 (4.3)	24 (43.6)	< 0.001	1 (1)	37 (12.9)	< 0.001
Diuretics, n (%)	28 (68)	30 (83.3)	0.207	24 (52)	31 (56.4)	0.674	55 (45)	122 (42.7)	0.701
Triple neurohormonal blockade, n (%)*	3 (7.3)	21 (58.3)	< 0.001	1 (2.2)	19 (34.5)	< 0.001	0 (0)	31 (10.8)	< 0.001

ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blocker; RAAS, renin-angiotensin-aldosterone system; BB, beta-blocker; MRA, mineralocorticoid receptor antagonist; *RAAS blocker (ACE inhibitor or ARB) + BB + MRA; p is the significance of differences between the groups.

50 % of those hospitalized with CHF [1, 13], but there has also been an increase in the number of patients with HFrEF in recent decades [14]. The above facts seem to reflect better treatment and prevention of CVD. In particular, some decrease in the incidence of CAD, absence of growth in the number of cases of acute MI as a cause of severe structural changes of myocardium leading to the development of systolic dysfunction of the heart, determines the decrease in the incidence among hospitalized patients with HFrEF. At the same time, the increase in risk factors and comorbidities leading to diastolic dysfunction of the heart, such as HHD, obesity, DM, AF, also contributes to the increase in the proportion of HFrEF in the structure of CHF. It should be noted that the increase in the percentage of patients with documented CHF among hospitalized patients may be related not only to changes in their numbers in the population, but also to clarification of the criteria for diagnosing CHF.

The number of patients with HFrEF may vary depending on the diagnostic criteria used, according to the results of several studies [15–17]. For example, in a previous study, the diagnosis of HFrEF based on medical records was confirmed in 80% of patients according to the 2018 OSSN/RCO/RNMOT criteria, including the presence of symptoms, LVEF≥50%, and additional echocardiographic criteria, and NT-proBNP was used as a mandatory criterion in only 38% of patients [18]. In this study, the presence of CHF was determined by the attending physician primarily based on the assessment of symptoms and signs of CHF and echocardiographic criteria of systolic or diastolic dysfunction of the heart; NT-proBNP was determined only in individual cases in routine clinical practice. Thus, the clarification of echocardiographic criteria for the diagnosis of diastolic dysfunction in current clinical guidelines likely contributed to the identification of more patients with HFrEF in the cohort of patients admitted to cardiology clinics in 2021.

Limitations

This study is limited by the fact that different approaches to verifying the diagnosis of CHF were used to enroll patients in 2002 and 2021, in accordance with the clinical guidelines and diagnostic criteria applicable at the time of inclusion. In addition, the lack of routine determination of NT-proBNP in CHF patients included in 2021 is also a limitation of the study, which was compensated by expert echocardiographic assessment of systolic and diastolic function of the heart.

Conclusion

In 2021, the percentage of patients with documented CHF in the cohort of patients hospitalized in cardiology clinics was 2 times higher than in 2002, with a preserved left ventricular ejection fraction phenotype prevailing in the structure of CHF. An increase in the prevalence of comorbidities in patients with CHF was observed over the twenty-year period analyzed. The frequency of prescribing pathogenetic evidence-based therapy has increased significantly by 2021, but its use remains inadequate even in CHF patients with reduced left ventricular ejection fraction.

No conflict of interest is reported.

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