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Chronic heart failure in the Russian Federation: what has changed over 20 years of follow-up? Results of the EPOCH-CHF study

Aim	To study the etiology and the dynamics of prevalence and mortality of CHF; to evaluate the treatment coverage of such patients in a representative sample of the European part of the Russian Federation for a 20-year period.
Material and methods	A representative sample of the European part of the Russian Federation followed up for 2002 through 2017 (n=19276); a representative sample of the population of the Nizhny Novgorod region examined in 1998 (n=1922).
Results	During the observation period since 2002, the incidence of major CHF symptoms (tachycardia, edema, shortness of breath, weakness) tended to decrease while the prevalence of cardiovascular diseases has statistically significantly increased. During the period from 1998 through 2017, the prevalence of I-IV functional class (FC) CHF increased from 6.1% to 8.2% whereas III-IV FC CHF increased from 1.8% to 3.1%. The main causes for the development of CHF remained arterial hypertension and ischemic heart disease; the role of myocardial infarction and diabetes mellitus as causes for CHF was noted. For the analyzed period, the number of treatment components and the coverage of basic therapy for patients with CHF increased, which probably accounts for a slower increase in the disease prevalence by 2007–2017. The prognosis of patients was unfavorable: in I-II FC CHF, the median survival was 8.4 (95% CI: 7.8–9.1) years and in III-IV FC CHF, the median survival was 3.8 (95% CI: 3.4–4.2) years.
Keywords	Clinical epidemiology; chronic heart failure; EPOCH-CHF; prevalence; prognosis; CHF portrait; treatment of CHF; ACEI; mineralocorticoid receptor antagonists; beta-blockers
For citation	Polyakov D.S., Fomin I.V., Belenkov Yu.N., Mareev V.Yu., Ageev F.T., Artemyeva E.G. et al. Chronic heart failure in the Russian Federation: what has changed over 20 years of follow-up? Results of the EPOCH-CHF study. Kardiologiia. 2021;61(4):4–14. [Russian: Поляков Д.С., Фомин И.В., Беленков Ю.Н., Мареев В.Ю., Агеев Ф.Т., Артемьева Е.Г. и др. Хроническая сердечная недостаточность в Российской Федерации: что изменилось за 20 лет наблюдения? Результаты исследования ЭПОХА–ХСН. Кардиология. 2021;61(4):4–14]
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ISSN 0022-9040. Kardiologiia. 2021;61(4). DOI: 10.18087/cardio.2021.4.n1628

Introduction

Chronic heart failure (CHF), which develops at the end of the cardiovascular disease continuum (CVDC), is characterized by a significantly increased risk of all-cause and cardiovascular mortality [1–3]. Until the 1980s, the unsatisfactory life expectancy of CHF patients was due to a deficiency of drug treatments affecting the prognosis, a failure to prevent the progression of myocardial injury, and a lack of surgical and electrophysiological treatments affecting survival in advanced CHF. This period also saw an increase in the prevalence of diseases that cause the development of CHF, resulting in its increased prevalence in the population [4, 5]. On the other hand, increased numbers of CHF patients are also due to advances in the treatment of coronary artery disease (CAD), arterial hypertension (AH), and diabetes mellitus (DM): improved prognosis of the underlying disease increases the life expectancy of these patients [6, 7].

About 40 years ago, physicians were able to influence the prognosis of a CHF patient for the first time [8]. Significant advances in treating patients with CHF at the population and individual levels with each new decade have mainly been associated with the more common use of the main drugs and changes in CHF treatment strategy [7, 9, 10]. Higher life expectancy is due to the development of disease management programs based on the formation of dedicated multidisciplinary teams to treat CHF [11–13].

The above-described phenomena increased the survival of the CHF patient population, which in turn increased the prevalence of this syndrome in developed countries [13–16], as well as changing the life expectancy and cause-of-death structure of CHF patients [17, 18].

In 2002–2017, the EPOCH-CHF epidemiological study was conducted in European Russia to assess changes in the prevalence of CHF and analyze the mortality of CHF patients [19]. The preliminary pilot project EPOCH-CHF was implemented in the Nizhny Novgorod region in 1998 and 2000 [20].

As well as analyzing the origin of CHF, the present article examines changes in its prevalence and efficacy of treatment (1998–2017) and estimates the prognosis for the defined cohort of CHF patients (2002–2017) based on the epidemiological surveys within the twenty-year investigation.

Objective

Investigate the origin of CHF, changes in its prevalence and mortality, and the treatment coverage of such patients in a representative sample of the European Russian population within a twenty-year period.

Material and methods

In 2002, the EPOCH-CHF epidemiological study was launched in European Russia. The representative sample included nine regions of the Russian Federation randomized from the 43 European Russian constituent territories and comprising 27.4% of the total European Russian population at that time. In 2002, 79.3 million lived in European Russia, while 21,750,827 people resided in the constituent territories included in the study. The study included the Nizhny Novgorod, Kirov, Orenburg, Ryazan, Saratov Regions, the Republics of Tatarstan and Chuvashia, as well as the Perm and Stavropol Krais.

The decision to study 10 epidemiological sites in each region determined the randomization step: the division by 10 of the population of a randomized region. Next, after listing the names of all the regions were alphabetically along with their populations, the ten sites in which the study was to be conducted were randomized.

If the number of residents of a settlement was a multiple of the randomization step, numerous sites were formed (mainly in large cities/regional capitals). Such step-by-step randomization allowed both urban and rural populations to be included in the regions of interest.

An outpatient clinic was randomized in each site, including four districts covered also selected randomly. In each district, a physician investigated 25 actual addresses (families) using step-by-step randomization. If two or more families living in a single apartment or house were not divided in the official residence list, such groupings were considered as one family. Thus, 100 families (four districts with 25 families) were surveyed and examined in each randomized site.

Each family was examined by a district physician, who was trained to fill in a survey record. A record was filled in for each family member above ten years for the survey, which was developed in cooperation with the State Research Center for Preventive Medicine of the Russian Ministry of Health (Moscow). The respondent's last name, first name, and middle name were coded under the Patient Rights Law following the Declaration of Helsinki. Each family member received his/her identification number, which remained the same during subsequent epidemiological surveys carried out under the EPOCH-CHF study.

The survey recorded included the respondent's sex, age, presence and history of cardiovascular disea-

ses (CVDs), cardiovascular risk factors, anthropometric data, hemodynamic indicators comprising blood pressure (BP) and resting heart rate, as well as cardiovascular therapy received at the time of examination. The physician was unable to influence the patient's answers and recorded the treatments of CVDs and DM according to oral information provided by the patient even if he/she was using a drug-free or non-recommended drug therapy [21].

The «soft» and «hard» criteria for CHF diagnosis were determined to analyze the sample of CHF patients. The «soft» criteria included a history of dyspnea during vigorous walking and CVDs [AH, CAD, myocardial infarction (MI), cerebrovascular accident (CVA)], as well as intermittent claudication, heart defects, and – in the subsequent surveys carried out in 2007 and 2017 – the presence of type 2 DM, and permanent atrial fibrillation (AF) in 2017. In contrast with previous studies, the analysis considered the presence of DM as a CVD in the 2002 survey. The dyspnea classification used in the EPOCH study is provided in the appendix. The «hard» criteria were CVDs, dyspnea, and tachycardia (HR 80 bpm or higher at rest), weakness, and swelling of any severity. The use of antihypertensive therapy at the respondent's examination and BP <140/90 mm Hg placed the patient in the AH group. The use of HR lowering drugs represented the epidemiological equivalent of tachycardia, while loop diuretics were the epidemiological equivalent of lower extremity edema.

In 2005, the hospital stage of the EPOCH-CHF study was conducted to confirm the diagnosis of CHF. At this stage of the study, respondents with CVDs, dyspnea when walking (grade 2 dyspnea according to the EPOCH score), and fatigue were admitted to hospitals. During this routine hospitalization, physicians performed clinical and laboratory examinations to verify the diagnosis of CHF. If a patient had clinical symptoms of CHF and at least one positive laboratory or clinical test showing cardiovascular disease or DM, as well as a positive 6-minute walk distance (6MWD) test, the diagnosis of CHF was confirmed [19, 22].

From 2003 to 2005, the hospital stage was implemented in four regions of European Russia: the Nizhny Novgorod, Ryazan, and Kirov Regions, as well as the Chuvash Republic. A total of 931 respondents from these four Russian regions were hospitalized, i.e., 80.7% of the total number of studied subjects having a suspected CHF diagnosis in this sample of the four Russian regions.

Due to the prevalence of CHF FC I–IV diagnosed under mild criteria at hospital being confirmed in 78.8% of cases, we were able to calculate the true prevalence of CHF in the Russian representative sample using the correction factor (– 21.2%). Thus, the actual prevalence of CHF FC I–IV (NYHA) in the European Russian representative sample was 6.8%. The diagnosis of CHF under the «hard» criteria was confirmed in 92.8% of cases; by applying the correction factor (– 7.2%), the true prevalence of CHF FC III–IV (NYHA) was established to be 2.1% [22].

The total size of the 2002 sample included 19,276 respondents. The investigators of the Voronezh and Orenburg regions declined to carry out a repeated survey in 2007. The sample used to form the cohort was reduced by the number of respondents of these regions (19,276–4,807=14,469 respondents). By 2017, due to natural population decrease and migration, as well as the administrative and territorial transformation of the therapeutic districts, the sample size was reduced to 11,453 respondents.

In 1998 and 2000, a pilot project was implemented to create and analyze a representative sample in the Nizhny Novgorod region. Since the randomization of apartments in all regions was the same, the findings on the CHF prevalence in the pilot sample will be added in the subsequent analyzes to the data of the main sample

In the formed sample with the new respondents included in the study in 2007, 11,453 respondents were followed up until 2017 (Table 1). Despite the relatively significant losses of respondents in 2007–2017, it can be assumed that the sample remained representative since it was replenished at each survey by newly arrived random respondents residing at the same addresses that were randomized in 2002.

The analysis of the cohort of 11,743 respondents and 2,781 deaths produced Kaplan-Mayer survival curves based on the presence or absence of CVDs since 2002. The mortality of CHF patients was analyzed separately depending on the severity of clinical signs corresponding to CHF functional classes: CHF FC I–IV under the «soft» criteria (CVDs and dyspnea grade 2 and higher) and CHF FC III–IV under the «hard» criteria.

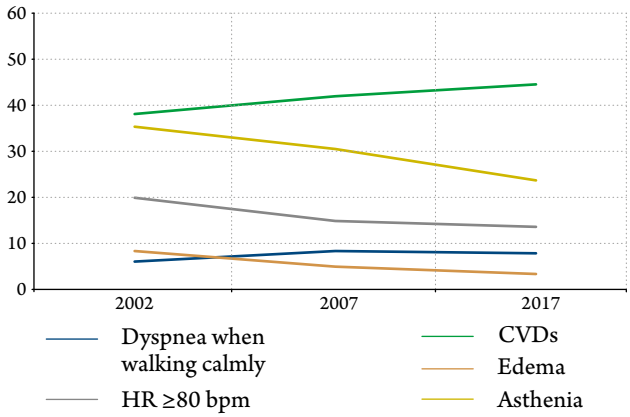
The patients were artificially divided into FC I–II and FC III–IV groups to form the cohort of mild patients with CHF FC I–II by calculating the difference between the number of patients with CHF FC I–IV and FC III–IV. Four cohorts were formed: non-CVD respondents, CVD patients without clinical

ISSN 0022-9040. Kardiologiia. 2021;61(4). DOI: 10.18087/cardio.2021.4.n1628

Table 1. Composition of the representative sample by epidemiological surveys over sixteen years

Year	Examined patients	Deceased patients	New respondents	Lost to follow-up
1998	1922 – pilot	–	–	–
2002	19276 (14469)	–	–	–
2007	14534	1620	738	924
2017	11453	1620+1888= 3550	1681	1360 (9.3%)

Figure 1. Changes in the prevalence of epidemiological criteria of CHF in the sample



Sign*	2002 (%)	2007 (%)	2017 (%)
Dyspnea	9.87	12.2	11.8
Edema	12.2	8.75	7.14
HR ≥80 bpm	23.9	18.8	17.8
Asthenia	39.5	34.5	27.7
CVD	42.3	46.4	49.8

* p value < 0.001 for all horizontal comparisons

signs of CHF, and two cohorts of patients with CHF FC I–II and FC III–IV.

The data were statistically processed using the R environment (R Core Team, 2020. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL: https://www.R-project.org/). In the given descriptive statistics, qualitative variables are presented as percentages, while the intergroup evaluation of the statistical significance of differences was carried out using the chi-squared test or Fischer's exact test. The survival analysis used the Kaplan–Meyer curves, and the statistical significance of intergroup differences was assessed using a log-rank test. The significance threshold for the statistical hypotheses was 0.05.

Results

From 2002 to 2017, changes in the prevalence of clinical symptoms in the general sample were observed from one epidemiological survey to another, which comprised the diagnostic criteria for CHF (Figure 1). We recorded an increase in the prevalence of dyspnea when walking from 9.9% to 11.8% ($p<0.001$) over time. The increase in the number of patients with severe dyspnea, which was especially evident between 2002 and 2007 (Figure 1), may be associated with the increased number of patients with CHF FC III–IV.

By 2017, the prevalence of tachycardia decreased among the respondents from 23.9% to 17.8% ($p<0.001$), lower extremity edema of any severity decreased from 12.2% to 7.1% ($p<0.001$), and asthenia of any severity was reduced from 39.5% to 27.7% ($p<0.001$). It is not impossible that these changes in the clinical course of the disease may be associated with a large treatment coverage, including beta-blockers (BBs), angiotensin-converting enzyme (ACE) inhibitors, and diuretics. The prevalence of CVDs in the sample increased from 42.3% to 49.8% ($p<0.001$) between 2002 and 2017.

Changes in the CHF prevalence in the representative sample are presented in Table 2. The prevalence of CHF was investigated in each epidemiological survey, including in 1998 (Nizhny Novgorod Region). From 1998 to 2007, there was a steady increase in the prevalence of CHF under the «soft» criteria (from 6.1% to 8.5%; $p<0.001$) and «hard» criteria (from 1.8% to 3.1%; $p<0.001$). There was no statistically significant change in the prevalence in 2017 from 2007, either by soft or «hard» criteria.

The analysis of the prevalence of potential causes of CHF showed that MI and DM were competing causes of CHF, as well as AH and CAD (Table 3).

Table 2. Changes in the prevalence of CHF in the European Russian representative sample in 2002–2017

Indicator	1998 (%)	2002 (%)*	2002 (%)*	2007 (%)	2007 (%)	2017 (%)	2017 (%)
FC I–II	4.3	5.89	–	7.35	–	7.08	–
FC III–IV	1.8	2.61	2.4	3.45	3.4	3.32	3.1
FC I–IV	6.1	8.5	6.7	10.8	8.5	10.4	8.2
CVDs without CHF	32.8	33.8	–	35.6	–	39.4	–

*, the first column for each year includes the prevalence of CHF by criteria used to select patients for validation: dyspnea grade 2, CVDs, and fatigue. The second column for each year is a figure using the conversion factor for CHF FC I–IV (–21.2%) and CHF FC III–IV (–7.2%).

Table 3. The main causes of CHF* in 1998–2017

Year	AH, %	CAD, %	MI, %	CVA, %	IC, %	DM, %	Defects, %	AF, %
1998	94.2	56.7	5.8	9.6	9.6	10.6	n/a	n/a
2002	93.2	63.7	14.5	12.6	9.5	12.6	3.7	n/a
2007	98.5	64.0	16.1	10.9	5.9	14.8	2.6	n/a
2017	98.7	63.3	15.8	10.6	4.5	16.6	3.1	12.3

* Criteria of CHF are CVDs and dyspnea grade 2 and above. AH – arterial hypertension; CAD – coronary artery disease; MI – myocardial infarction; CVA – cerebrovascular accident; IC – intermittent claudication; DM – diabetes mellitus; AF – atrial fibrillation.

Table 4. The main causes of CHF in 2017 among respondents with* and without CHF

Cause, %	AH	CAD	MI	CVA	IC	DM	Defects	PAF
No CHF	42.1	6.9	1.2	1.5	0.7	3.2	0.8	0.7
CHF	98.7	63.3	15.8	10.6	4.5	16.6	3.1	12.3
p	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**
CHF FC I–II	98.2	57.5	15.2	10.4	3.4	15.0	2.4	10.1
CHF FC III–IV	100	77.9	17.4	11.1	7.1	20.5	4.7	17.9
p	**0.005**	**<0.001**	**0.04**	**0.24**	**0.001**	**0.02**	**0.04**	**<0.001**

*Criteria of CHF are CVDs and dyspnea grade 2 and above. AH – arterial hypertension; CAD – coronary artery disease; MI – myocardial infarction; CVA – cerebrovascular accident; IC – intermittent claudication; DM – diabetes mellitus; PAF – persistent atrial fibrillation.

The analysis of the prevalence of the main causes of CHF was performed among patients with and without documented CHF. The sample was divided into groups of patients with CHF FC I–II and CHF FC III–IV. There was a statistically significant increase in the prevalence of all comorbidities causing CHF in respondents with CHF compared to CVD patients without CHF. The analysis of the origin of CHF in patients with FC I–II compared to that of those with FC III–IV showed that all the CHF causes of interest, except for CVA, are more common in patients with CHF FC III–IV (Table 4) to a statistically significant extent.

The structure of treatment with CHF modifying drugs was analyzed between 1998 and 2017 in patients with FC III–IV. The treatment coverage of at least one of the drugs recommended to treat CHF reached 97.1% by 2017 (Table 5 and 6).

We established a significant increase in the frequency of using ACE inhibitors in the population of patients with CHF FC III–IV from 24.3% to 78.6% of cases from 1998 to 2007.

Within the ten year period from 2007, an artificial replacement of ACE inhibitors by angiotensin II receptor blockers (ARBs) occurred. The rate of using the latter increased to 24.5% of cases during this period of observation. Although the total proportion of respondents taking ACE inhibitors or ARBs reached 92.7%, there was a negative trend in the rate of using ACE inhibitors in patients with CHF FC III–IV and an increase in the rate of administering ARBs during the last ten years (Table 5).

Table 5. Frequency of using the disease-modifying drugs in patients with CHF FC III–IV in the European Russian representative sample

Class of drugs	Administration rate, %			
	1998	2002 г.	2007 г.	2017 г.
ACE inhibitors	24.3	53.9	78.6	68.2
ARBs	0	0	3.2	24.5
BBs	15.3	31.6	61.9	75.3
MRA	0	2.2	6.2	25.3

ACE – angiotensin-converting enzyme; ARB – angiotensin II receptor blocker; BB – beta-blocker; MRA – mineralocorticoid receptor antagonist.

The rate of taking BBs in patients with CHF FC III–IV increased four times (from 15.3% to 75.3%) over the observation period; however, in 2017, every third patient taking BBs used a beta-blocker not recommended for the treatment of CHF (metoprolol tartrate, atenolol). The percentage of respondents receiving mineralocorticoid receptor antagonists (MRAs) increased ten times from 2.2% to 25.3% (Table 4).

Drug-free therapies and those involving the use of only one main drug were analyzed. This analysis showed that the number of patients with CHF FC III–IV who did not take any CHF-modifying drugs decreased twelve times over 15 years (Table 5). In 2017, every fourth patient with CHF took only one disease-modifying drug (23.5%); in just over half of the cases

ISSN 0022-9040. Kardiologiia. 2021;61(4). DOI: 10.18087/cardio.2021.4.n1628

(12.4%), it was a RAAS blocker. Monotherapy with beta-blockers decreased from 11.7% to 5.3% during the observation period, while MRA monotherapy in the sample of CHF patients occurred only sporadically (Table 6).

Year-on-year, the number of patients taking two disease-modifying drugs increased from 19.9% (2002) to 54.6% (2017). The majority of CHF patients received dual disease-modifying treatment using ACE inhibitors and BBs. From 2002 to 2007, there was a marked increase in the percentage of patients taking two recommended drugs up to 52.9%. The number of CHF patients receiving the dual disease-modifying therapy did not increase in the next ten years (54.6%) (Table 6). The analysis of the drug treatment conformity with clinical guidelines showed that only 49.2% of patients received recommended combinations of ACE inhibitors/ARBs plus BBs in 2017.

The percentage of patients receiving triple therapy increases in all three epidemiological surveys, from 0.8% to 19%. In 2007, the ratio of ACE inhibitors to ARBs was 17:1, and in 2017, this ratio reached 3:1, which was observed in almost all the combination regimens in the study sample (Table 6).

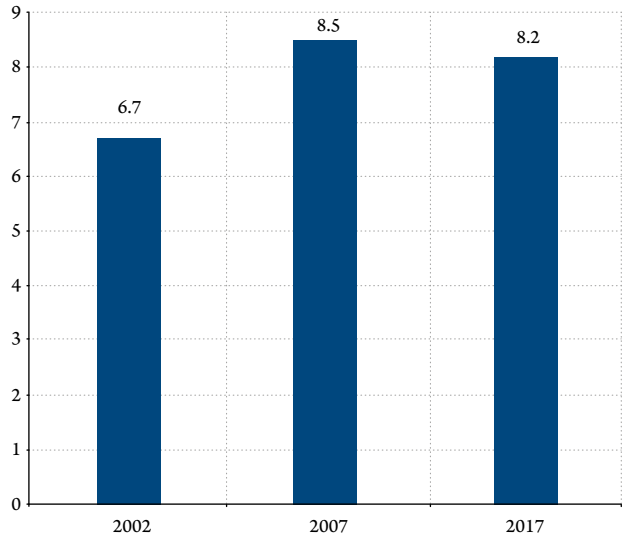
Figure 2 shows the Caplan – Mayer survival curves of the four respondent cohorts studied from 2002 to 2017: patients without CVDs, CVD patients without CHF, and two samples of patients with CHF FC I–II or CHF FC III–IV. The prognosis and life expectancy were the worst in patients with CHF FC III–IV and slightly better in patients with CHF FC I–II. Median survival in patients with CHF FC I–II was 8.4 (95% CI: 7.8–9.1) years, with a maximum survival time of 15.3 years; the total annual mortality rate was 4.8%.

The median survival time in severe patients with CHF FC III–IV was 3.8 (95% CI: 3.4–4.2) years, which turned out to be 2.2 times worse compared to patients with CHF I–II FC. The maximum survival probability for patients with CHF FC III–IV was only 9.8 years. The annual rate of all-cause mortality was 10.2% in this group.

The prognosis for CVD patients without CHF and those without CVD was statistically significantly better. All survival curves separated during the first year of observation (Figure 3).

Thus, the twenty years of observation of the representative sample in European Russia showed a statistically significant increase in the number of patients with CHF due to an increase in the number of patients with FC I–II with a slight slowdown of the increase in the number of patients with FC III–IV. The treatment coverage increased significantly and tended toward the best possible combination of disease-modifying drugs.

Figure 2. Prevalence of CHF in Russia*



* The following criteria were used in the figure: CVDs, dyspnea grade 2 and higher, asthenia, conversion factor for CHF FC I–IV (–21.2%) and CHF FC III–IV (–7.2%).

Table 6. Combination therapy with the disease-modifying drugs in patients with CHF FC III–IV

Classes of disease-modifying drugs	Administration rate, %		
	2002 r.	2007 r.	2017 r.
No disease-modifying therapy	**33.8%**	**8.0%**	**2.9%**
Monotherapy	**45.5%**	**36.7%**	**23.5%**
ACE inhibitors	33.6	27.5	12.4
ARBs	0	0	5.0
BBs	11.7	8.0	5.3
MRA	0.2	1.2	0.8
Dual therapy	**19.9%**	**52.9%**	**54.6%**
ACE inhibitor + BB	18.7	47.3	33.9
ARB + BB	0	3.0	15.3
ACE inhibitor + MRA	0.8	1.4	3.1
ARB + MRA	0	0	0.5
BB + MRA	0.4	1.2	1.8
Triple therapy	**0.8%**	**2.4%**	**19%**
ACE inhibitor + BB + MRA	0.8	2.4	15.2
ARB + BB + MRA	0	0	3.8

Discussion

The 20-year observation in the representative sample of European Russia comprised the analysis of three epidemiological surveys. Based on the formed

cohort from the representative sample, questions about the prognosis for CHF patients were considered depending on the severity of the syndrome.

The prevalence of CHF in the representative sample of European Russia increased with each subsequent epidemiological survey. The increase in the prevalence of CHF in the «soft» criteria subgroup (FC I–IV) was more pronounced than in the «hard» criteria subgroup (FC III–IV). For the twenty years of observation, the number of CHF patients of any FC increased by 2.1% (from 6.1% to 8.2%), which is 3.1 million people based on the general Russian population as of 2019, and the estimated Russian sample of CHF patients can reach 12 million patients with any FC [23].

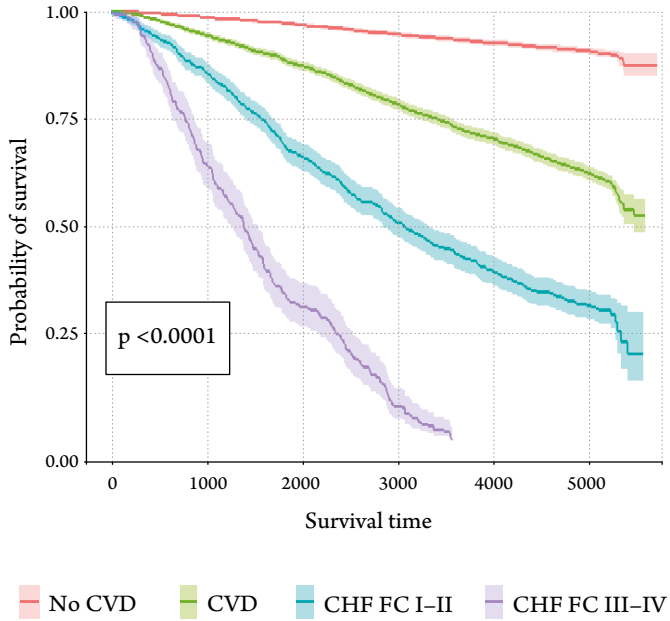
The estimated number of patients with CHF FC III–IV who have the worst life expectancy increased by 1.3% (from 1.8% to 3.1%) during the twenty-year study and amounted to 4.5 million people in 2017 [23]. The failure to detect a statistically significant increase in the number of patients under the «hard» criteria of CHF over the past ten years may indicate that the rate of increase in the number of patients with new-onset severe CHF was the same as the mortality rate in this category of patients.

The prevalence of CHF in the representative sample was determined in the EPOCH study by clinical and anamnestic data [19, 21, 22], similar to the clinical symptom criteria used for the diagnosis of CHF in the population studies of the early 1970–80s. Since the increased administration of the analyzed drugs was observed in the representative sample of CVD patients, the clinical criteria used for the diagnosis of CHF may lose their sensitivity in the current real-world clinical practice and may only be used at the stage of the provisional diagnosis of CHF.

Since the early 2010s, natriuretic peptides have been evaluated and heart sonography performed in real-world clinical practice to confirm the diagnosis of CHF [14, 24, 25]. In patients with non-informative echocardiographic data, MRI is the best additional imaging technique due to the high image quality [26].

Moreover, while the presence of symptoms and/or signs of CHF and left ventricular ejection fraction (LVEF) <40% are the only criteria required to diagnose heart failure with reduced ejection fraction (HFrEF), there are several diagnostic criteria of heart failure with preserved ejection fraction (HFpEF). For example, according to the 2013 AHA/ACC guideline, HFpEF is diagnosed in patients with preserved LVEF having symptoms or signs of CHF [27]. At the same time, according to the ESC 2016 criteria, LVEF ≥50%, additional echocardiographic indicators and increased

Figure 3. Probability of survival of respondent within an 18-year observation period



levels of brain natriuretic peptide (BNP) are necessary diagnostic criteria [25]. Ho et al. [28] showed that, among 461 patients with dyspnea and LVEF ≥50%, HFpEF was confirmed in 416 (90%) patients under the AHA/ACC 2013 criteria but only in 205 (44%) patients under the ESC 2016 criteria. According to a small Russian study, HFpEF diagnosed in hospital was confirmed in 80% of cases using the criteria of the Russian Heart Failure Society, the Russian Society of Cardiology, and the Russian Scientific Medical Society of Internal Medicine [29] (LVEF ≥50% + symptoms and/or signs + additional echocardiographic criteria) and in 37% of cases under the ESC 2016 criteria including the same criteria and BNP [30]. It should be noted that additional scores have been developed recently for the diagnosis of HFpEF, which may include BNP [31] or not [32]. The ESC 2016 criteria and new scores produce different numbers of patients with HFpEF [33, 34], which indicates the lack of a unified diagnosis concept.

The prevalence of CHF continues to increase worldwide due to the growing number of patients with CVDs [1, 4, 7]. The percentage of patients with severe CHF is also increasing globally [6, 35, 36]. The incidence of CHF in patients older than 45 was 7.9 and 6.0 per 1,000 person-years in two cohorts NHLBI's and ARIC, respectively. In the CHS study, this figure was higher, reaching 21–29 per 1,000 of the population [37]. The Kaiser Permanente site for Health Research (KPCHR) study, which compared two cohorts of patients created from 1970 to 1974 and from 1990 to 1994, observed an increase in the number of patients

ISSN 0022-9040. Kardiologiia. 2021;61(4). DOI: 10.18087/cardio.2021.4.n1628

with CHF in the groups above 65 years [38]. The Olmsted County study, conversely, showed a decrease in the incidence of CHF along with reduced and preserved left ventricular ejection fraction from 2000 to 2010 [39].

The results of our study indicate an increasing contribution of AH, CAD, history MI, persistent AF, and DM in the development of CHF, which is also associated with significant achievements and successes in their treatment [6, 7, 40]. Better organization of medical care in acute coronary syndrome and CVA resulted in a significant decrease in mortality and a simultaneous increase in the development of CHF at the population level [38, 41].

The growing prevalence of CHF in the Russian Federation may be attributed to the number of patients with a history of acute cardiovascular complications and patients receiving poor treatment.

The survival analysis carried out in the representative sample independently of CHF FC showed that the risks of fatal outcomes in the 1970–80s were similar in the Russian Federation to those obtaining in Europe and the USA, the period before the active use of neurohormonal blockers [17, 42]. The mean life expectancy was 8.1 years in patients with CHF FC I–II and 3.7 years in severe patients with CHF FC III–IV. The analysis of two US cohorts over twenty years (1970–1974 and 1990–1994) showed that while incidence increased by 14% (95% CI: 2–28%), risk of death decreased by 33% (95% CI: 14–48%) in male patients and 24% (95% CI: 1–43%) in female patients [38]. There were no evident trends in decreasing mortality rates in other cohort studies over the past thirty years in patients with CHF FC II–IV [4, 43], which was associated with suboptimal treatment coverage.

We observe a significant improvement in the prognosis and life expectancy of patients with CHF worldwide, which is associated with the administration of neurohumoral blockers, active use of beta-blockers, and surgeries [10, 44–46].

The presented study revealed positive trends in increasing the treatment coverage of CHF patients. In the past ten years (2007–2017), the growth of treatment coverage slowed down in European Russia.

It appears in the initial analysis of treatment data that the therapy of CHF in Russia conforms with clinical guidelines, the threshold of treatment coverage reached almost 60%, and there is a positive trend toward a higher percentage of patients receiving the combination therapy of CHF. Interestingly, only 73.6% of patients took a combination of two or three disease-modifying drugs. Every fourth patient used an ARB, but not an ACE inhibitor. It is unlikely that there are so many patients with ACE inhibitor intolerance in the Russian Federation. There is a trend of increasing use of ARBs in patients with CHF, which is due to the physicians' real-world practice and the artificial substitution of the diagnosis of heart failure for arterial hypertension.

The use of very low doses of drugs is undoubtedly a shortcoming of the real-world clinical practice in the Russian Federation, which is associated not only with low treatment compliance but also with low activity of physicians in real-world clinical practice [15].

There has been a dramatic change in the treatment of CHF patients in Europe in recent years. In the contemporary analyzed cohorts, more patients exceed 50% of the recommended doses of the disease-modifying drugs, as well as actively using combination therapies, which influences prognosis and life expectancy [10, 47, 48]. The impossibility of improving prognosis and life expectancy by administering low doses of disease-modifying drugs was confirmed in many international studies [10, 47]. Thus, the prospect of achieving rapid changes in real-world clinical practice by developing specialized medical care for CHF patients is shown in the international and Russian studies [2, 49, 50].

Today, the prognosis for CHF patients remains poor because life expectancy is very short irrespective of CHF FC; this explains why the management of CHF patients should be modified as quickly as possible. To that end, it is necessary to understand that CHF is one of the main causes both of all-cause and cardiovascular mortality. Changes in methods of recording fatal outcomes are necessary since death often occurs as a result of decompensated HF or sudden cardiac death in high FC CHF, with the cause of death being established according to the etiological diagnosis. By presenting the cause of HF as the main cause of death, we have an opportunity to more accurately define the structure of cardiovascular mortality in the Russian Federation. This will require changes at the national level of statistical analysis using the I50 code to indicate cause of death.

New approaches should be developed for earlier and more accurate diagnosis of CHF, followed by the development of CHF progression prevention programs at the population level. Effective monitoring of CHF patient management and accurate implementation of the national clinical guidelines for the treatment of heart failure is possible only by establishing a register of patients with CVDs and analyzing mortality rates

for each treatment district. This will have a significant effect on mortality and lead to increased life expectancy in the Russian population.

Conclusions

1. The prevalence of CHF increased in the Russian Federation from 6.1% to 8.2% during the twenty-year observation.
2. The portrait of a CHF patient has changed over twenty years: the prevalence of tachycardia has decreased from 23.9% to 17.8%, lower extremity edema of any severity – from 12.2% to 7.1%, asthenia of any severity – from 39.5% to 27.7%, which is associated with an extensive treatment coverage with RAAS blockers, beta-blockers, and MRAs.
3. Compared to CVD patients without CHF, patients with CHF have more comorbidities that can cause and/or exacerbate CHF.
4. The median survival time was 8.4 years in patients with CHF FC I–II and 3.8 years in patients with CHF FC III–IV; this indicates a poor prognosis for patients with CHF of any functional class.
5. The coverage of CHF patients with combined disease-modifying therapy is low; moreover, ARBs are overused.

Funding

All-Russian public organization
«Society of Specialists in Heart Failure».

No conflict of interest is reported.

The article was received on 16/01/2020

Appendix. Classification of dyspnea in the EPOCH study:

~ when walking fast (FC I)
~ when walking calmly (FC II)
~ that makes one stop when dressing (FC III)
~ at rest or with little exercise (FC IV)

REFERENCES

1. Tsao CW, Lyass A, Enserro D, Larson MG, Ho JE, Kizer JR et al. Temporal Trends in the Incidence of and Mortality Associated with Heart Failure with Preserved and Reduced Ejection Fraction. JACC: Heart Failure. 2018;6(8):678–85. DOI: 10.1016/j.jchf.2018.03.006
2. Vinogradova N.G., Polyakov D.S., Fomin I.V. Analysis of mortality in patients with heart failure after decompensation during long-term follow-up in specialized medical care and in real clinical practice. Kardiologiia. 2020;60(4):91–100. [Russian: Виноградова Н.Г., Поляков Д.С., Фомин И.В. Анализ смертности у пациентов с ХСН после декомпенсации при длительном наблюдении в условиях специализированной медицинской помощи и в реальной клинической практике. Кардиология. 2020;60(4):91-100]. DOI: 10.18087/cardio.2020.4.n1014
3. Shah KS, Xu H, Matsouaka RA, Bhatt DL, Heidenreich PA, Hernandez AF et al. Heart Failure with Preserved, Borderline, and Reduced Ejection Fraction. Journal of the American College of Cardiology. 2017;70(20):2476–86. DOI: 10.1016/j.jacc.2017.08.074
4. Gerber Y, Weston SA, Enriquez-Sarano M, Berardi C, Chamberlain AM, Manemann SM et al. Mortality Associated with Heart Failure After Myocardial Infarction: A Contemporary Community Perspective. Circulation: Heart Failure. 2016;9(1):e002460. DOI: 10.1161/CIRCHEARTFAILURE.115.002460
5. Boytsov S.A., Balanova Yu.A., Shal'nova S.A., Deev A.D., Artamonova G.V., Gatagonova T.M. et al. Arterial hypertension among persons aged 25-64: prevalence, awareness, treatment and control. By the data from ECCD. Cardiovascular Therapy and Prevention. 2014;13(4):4–14. [Russian: Бойцов С.А., Баланова Ю.А., Шальнова С.А., Деев А.Д., Артамонова Г.В., Гатагонова Т.М. и др. Артериальная гипертония среди лиц 25-64 лет: распространенность, осведомленность, лечение и контроль по материалам исследования ЭССЕ. Кардиоваскулярная терапия и профилактика. 2014;13(4):4-14]. DOI: 10.15829/1728-8800-2014-4-4-14
6. Xanthakis V, Enserro DM, Larson MG, Wollert KC, Januzzi JL, Levy D et al. Prevalence, Neurohormonal Correlates, and Prognosis of Heart Failure Stages in the Community. JACC: Heart Failure. 2016;4(10):808–15. DOI: 10.1016/j.jchf.2016.05.001
7. Benjamin EJ, Muntner P, Alonso A, Bittencourt MS, Callaway CW, Carson AP et al. Heart Disease and Stroke Statistics–2019 Update: A Report from the American Heart Association. Circulation. 2019;139(10):e56–528. DOI: 10.1161/CIR.0000000000000659
8. The Consensus Trial Study Group*. Effects of Enalapril on Mortality in Severe Congestive Heart Failure. New England Journal of Medicine. 1987;316(23):1429–35. DOI: 10.1056/NEJM198706043162301
9. DeVore AD, Thomas L, Albert NM, Butler J, Hernandez AF, Patterson JH et al. Change the management of patients with heart failure: Rationale and design of the CHAMP-HF registry. American Heart Journal. 2017; 189:177–83. DOI: 10.1016/j.ahj.2017.04.010
10. Komajda M, Böhm M, Borer JS, Ford I, Tavazzi L, Pannaux M et al. Incremental benefit of drug therapies for chronic heart failure with reduced ejection fraction: a network meta-analysis. European Journal of Heart Failure. 2018;20(9):1315–22. DOI: 10.1002/ejhf.1234
11. Gelbrich G, Störk S, Kreißl-Kemmer S, Faller H, Prettin C, Heuschmann PU et al. Effects of structured heart failure disease management on mortality and morbidity depend on patients' mood: results from the Interdisciplinary Network for Heart Failure Study: Effects of structured HF management depend on patients' mood. European Journal of Heart Failure. 2014;16(10):1133–41. DOI: 10.1002/ejhf.150
12. Van Spall HGC, Rahman T, Mytton O, Ramasundarahettige C, Ibrahim Q, Kabali C et al. Comparative effectiveness of transitional care services in patients discharged from the hospital with heart failure: a systematic review and network meta-analysis: Comparative effectiveness of transitional care services in patients hospitalized with heart failure. European Journal of Heart Failure. 2017;19(11):1427–43. DOI: 10.1002/ejhf.765
13. Bragazzi NL, Zhong W, Shu J, Abu Much A, Lotan D, Grupper A et al. Burden of heart failure and underlying causes in 195 countries and territories from 1990 to 2017. European Journal of Preventive Cardiology. 2021;zwaa147. [Epub ahead of print]. DOI: 10.1093/eurjpc/zwaa147
14. Groenewegen A, Rutten FH, Mosterd A, Hoes AW. Epidemiology of heart failure. European Journal of Heart Failure. 2020;22(8):1342–56. DOI: 10.1002/ejhf.1858

ISSN 0022-9040. Kardiologiia. 2021;61(4). DOI: 10.18087/cardio.2021.4.n1628

15. Fomin I.V. Chronic heart failure in Russian Federation: what do we know and what to do. Russian Journal of Cardiology. 2016; 8:7–13. [Russian: Фомин И.В. Хроническая сердечная недостаточность в Российской Федерации: что сегодня мы знаем и что должны делать. Российский Кардиологический Журнал. 2016; 8:7-13]. DOI: 10.15829/1560-4071-2016-8-7-13
16. Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE, Colvin MM et al. 2017 ACC/AHA/HFSA Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. Circulation. 2017;136(6):e137–61. DOI: 10.1161/CIR.0000000000000509
17. Taylor CJ, Ordóñez-Mena JM, Roalfe AK, Lay-Flurrie S, Jones NR, Marshall T et al. Trends in survival after a diagnosis of heart failure in the United Kingdom 2000-2017: population based cohort study. BMJ. 2019; 364:l223. DOI: 10.1136/bmj.l223
18. Di Tano G, De Maria R, Gonzini L, Aspromonte N, Di Lenarda A, Feola M et al. The 30-day metric in acute heart failure revisited: data from IN-HF Outcome, an Italian nationwide cardiology registry. European Journal of Heart Failure. 2015;17(10):1032–41. DOI: 10.1002/ejhf.290
19. Fomin I.V., Belenkov Yu.N., Mareev V.Yu., Ageev F.T., Badin Yu.V., Galyavich A.S. et al. Prevalence of CHF in European part of the Russian Federation: data from EPOCH-CHF. Russian Heart Failure Journal. 2006;7(1):4–7. [Russian: Фомин И. В., Беленков Ю.Н., Мареев В.Ю., Агеев Ф.Т., Бадин Ю.М., Галявич А.С. и др. Распространенность хронической сердечной недостаточности в Еверопейской части Российской Федерации. Данные ЭПОХА–ХСН. Журнал Сердечная Недостаточность. 2006;7(1):4-7.]
20. Shechrbinina E.V., Badin Yu.V., Vaysberg A.R. Dynamics of the etiological causes of CHF formation in a representative sample of the Nizhny Novgorod region over 9 years of follow-up (1998-2007). All-Russian Conference of CHF: "Heart failure, 2007". – M., 2007. – P. 38. [Russian: Щербинина Е.В., Бадин Ю.В., Вайсберг А.Р. Динамика этиологических причин формирования ХСН в репрезентативной выборке Нижегородской области за 9 лет наблюдения (1998–2007 гг.). Всероссийская конференция ОССН: «Сердечная недостаточность, 2007 год». – М., 2007. – С.38]
21. Mareev V.Yu., Belenkov Yu.N., Ageev F.T., Fomin I.V., Chochlov R.A., Galiavich A.S. et al. The first results of Russian epidemiological studies with CHF (EPOCHA-CHF). Russian Heart Failure Journal. 2003;4(1):17–8. [Russian: Мареев В.Ю., Беленков Ю.Н., Агеев Ф.Т., Фомин И.В., Хохлов Р.А., Галявич А.С. и др. Первые результаты Российского эпидемиологического исследования по ХСН (ЭПОХА-ХСН). Журнал Сердечная Недостаточность. 2003;4(1):17-8]
22. Belenkov Yu.N., Mareev V.Yu., Ageev F.T., Fomin I.V., Badin Yu.V., Polyakov D.S. et al. Veritable prevalence of CHF in the European part of Russian Federation (EPOCHA trial, hospital stage). Russian Heart Failure Journal. 2011;12(2):63–8. [Russian: Беленков Ю.Н., Мареев В.Ю., Агеев Ф.Т., Фомин И.В., Бадин Ю.В., Поляков Д.С. и др. Истинная распространенность ХСН в Европейской части Российской Федерации (ЭПОХА, госпитальный этап) Журнал Сердечная Недостаточность. 2011;12(2):63-8]
23. The World Bank. Population, total. Demographic Statistics. [Internet] Available at: https://data.worldbank.org/indicator/SP.POP.TOTL
24. Crespo-Leiro MG, Metra M, Lund LH, Milicic D, Costanzo MR, Filippatos G et al. Advanced heart failure: a position statement of the Heart Failure Association of the European Society of Cardiology: Advanced heart failure: HFA position statement. European Journal of Heart Failure. 2018;20(11):1505–35. DOI: 10.1002/ejhf.1236
25. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JGF, Coats AJS et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. European Heart Journal. 2016;37(27):2129–200. DOI: 10.1093/eurheartj/ehw128
26. Knuuti J, Wijns W, Saraste A, Capodanno D, Barbato E, Funck-Brentano C et al. 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes. European Heart Journal. 2020;41(3):407–77. DOI: 10.1093/eurheartj/ehz425
27. Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE, Drazner MH et al. 2013 ACCF/AHA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation. 2013;128(16):e240-327. DOI: 10.1161/CIR.0b013e31829e8776
28. Ho JE, Zern EK, Wooster L, Bailey CS, Cunningham T, Eisman AS et al. Differential Clinical Profiles, Exercise Responses, and Outcomes Associated With Existing HFpEF Definitions. Circulation. 2019;140(5):353–65. DOI: 10.1161/CIRCULATIONAHA.118.039136
29. Mareev V.Yu., Fomin I.V., Ageev F.T., Begrambekova Yu.L., Vasyuk Yu.A., Garganeeva A.A. et al. Russian Heart Failure Society, Russian Society of Cardiology. Russian Scientific Medical Society of Internal Medicine Guidelines for Heart failure: chronic (CHF) and acute decompensated (ADHF). Diagnosis, prevention and treatment. Kardiologiia. 2018;58(6S):8–158. [Russian: Мареев В.Ю., Фомин И.В., Агеев Ф.Т., Беграмбекова Ю.Л., Васюк Ю.А., Гарганеева А.А. и др. Клинические рекомендации ОССН–РКО–РНМОТ. Сердечная недостаточность: хроническая (ХСН) и острая декомпенсированная (ОДСН). Диагностика, профилактика и лечение. Кардиология. 2018;58(6S):8-158]. DOI: 10.18087/cardio.2475
30. Mareev Yu.V., Garganeeva A.A., Tukish O.V., Rebrova T.Yu., Anikina D.V., Mareev V.Yu. Difficulties in diagnosis of heart failure with preserved ejection fraction in clinical practice: dissonance between echocardiography, NTproBNP and H2HFPEF score. Kardiologiia. 2020;59(12S):37–45. [Russian: Мареев Ю.В., Гарганеева А.А., Тукиш О.В., Реброва Т.Ю., Аникина Д.В., Мареев В.Ю. Сложности в диагностике сердечной недостаточности с сохраненной фракцией выброса в реальной клинической практике: диссонанс между клиникой, эхокардиографическими изменениями, величиной натрийуретических пептидов и шкалой H2FPEF. Кардиология. 2019;59(12S):37–45]. DOI: 10.18087/cardio.n695
31. Pieske B, Tschöpe C, de Boer RA, Fraser AG, Anker SD, Donal E et al. How to diagnose heart failure with preserved ejection fraction: the HFA–PEFF diagnostic algorithm: a consensus recommendation from the Heart Failure Association (HFA) of the European Society of Cardiology (ESC). European Heart Journal. 2019;40(40):3297–317. DOI: 10.1093/eurheartj/ehz641
32. Reddy YNV, Carter RE, Obokata M, Redfield MM, Borlaug BA. A Simple, Evidence-Based Approach to Help Guide Diagnosis of Heart Failure With Preserved Ejection Fraction. Circulation. 2018;138(9):861–70. DOI: 10.1161/CIRCULATIONAHA.118.034646
33. Selvaraj S, Myhre PL, Vaduganathan M, Claggett BL, Matsushita K, Kitzman DW et al. Application of Diagnostic Algorithms for Heart Failure With Preserved Ejection Fraction to the Community. JACC: Heart Failure. 2020;8(8):640–53. DOI: 10.1016/j.jchf.2020.03.013
34. Gudieva Kh.M., Safarova A.F., Kobalava Zh.D. Use of the HFA-PEFF algorithm for diagnosis of heartfailure with preserved left ventricular ejection fraction. Clinical pharmacology and therapy. 2020;29(2):47–50. [Russian: Гудиева Х.М., Сафарова А.Ф., Кобалава Ж.Д. Применение алгоритма HFA-PEFF для диагностики сердечной недостаточности с сохраненной фракцией выброса левого желудочка. Клиническая фармакология и терапия. 2020;29(2):47-50]. DOI: 10.32756/0869-5490-2020-2-47-50
35. Bjork JB, Alton KK, Georgiopoulou VV, Butler J, Kalogeropoulos AP. Defining Advanced Heart Failure: A Systematic Review of Criteria Used in Clinical Trials. Journal of Cardiac Failure. 2016;22(7):569–77. DOI: 10.1016/j.cardfail.2016.03.003
36. Fang JC, Ewald GA, Allen LA, Butler J, Westlake Canary CA, Colvin-Adams M et al. Advanced (Stage D) Heart Failure: A Statement From the Heart Failure Society of America Guidelines Committee. Journal of Cardiac Failure. 2015;21(6):519–34. DOI: 10.1016/j.cardfail.2015.04.013

37. Huffman MD, Berry JD, Ning H, Dyer AR, Garside DB, Cai X et al. Lifetime Risk for Heart Failure Among White and Black Americans: cardiovascular lifetime risk pooling project. Journal of the American College of Cardiology. 2013;61(14):1510–7. DOI: 10.1016/j.jacc.2013.01.022
38. Barker WH. Changing Incidence and Survival for Heart Failure in a Well-Defined Older Population, 1970-1974 and 1990-1994. Circulation. 2006;113(6):799–805. DOI: 10.1161/CIRCULATIONAHA.104.492033
39. Gerber Y, Weston SA, Redfield MM, Chamberlain AM, Manemann SM, Jiang R et al. A contemporary appraisal of the heart failure epidemic in Olmsted County, Minnesota, 2000 to 2010. JAMA Internal Medicine. 2015;175(6):996–1004. DOI: 10.1001/jamainternmed.2015.0924
40. Bibbins-Domingo K, Pletcher MJ, Lin F, Vittinghoff E, Gardin JM, Arynchyn A et al. Racial Differences in Incident Heart Failure among Young Adults. New England Journal of Medicine. 2009;360(12):1179–90. DOI: 10.1056/NEJMoa0807265
41. Chen J, Normand S-LT, Wang Y, Krumholz HM. National and Regional Trends in Heart Failure Hospitalization and Mortality Rates for Medicare Beneficiaries, 1998-2008. JAMA. 2011;306(15):1669–78. DOI: 10.1001/jama.2011.1474
42. Alehagen U, Benson L, Edner M, Dahlström U, Lund LH. Association between use of statins and mortality in patients with heart failure and ejection fraction of ≥50. Circulation. Heart Failure. 2015;8(5):862–70. DOI: 10.1161/CIRCHEARTFAILURE.115.002143
43. Kotecha D, Flather MD, Altman DG, Holmes J, Rosano G, Wikstrand J et al. Heart Rate and Rhythm and the Benefit of Beta-Blockers in Patients With Heart Failure. Journal of the American College of Cardiology. 2017;69(24):2885–96. DOI: 10.1016/j.jacc.2017.04.001
44. McMurray JJV, Packer M, Desai AS, Gong J, Lefkowitz M, Rizkala AR et al. Baseline characteristics and treatment of patients in Prospective comparison of ARNI with ACEI to Determine Impact on Global Mortality and morbidity in Heart Failure trial (PARADIGM-HF). European Journal of Heart Failure. 2014;16(7):817–25. DOI: 10.1002/ejhf.115
45. Fiuzat M, Wojdyla D, Pina I, Adams K, Whellan D, O'Connor CM. Heart Rate or Beta-Blocker Dose? Association With Outcomes in Ambulatory Heart Failure Patients With Systolic Dysfunction: Results From the HF-ACTION Trial. JACC: Heart Failure. 2016;4(2):109–15. DOI: 10.1016/j.jchf.2015.09.002
46. Ferrari R. A step further with ivabradine: SIGNIfY (Study assessInG the morbidity-mortality beNefits of the If inhibitor ivabradine in patients with coronarY artery disease). European Heart Journal Supplements. 2009;11(Suppl D):D19–27. DOI: 10.1093/eurheartj/sup014
47. Rossignol P, Hernandez AF, Solomon SD, Zannad F. Heart failure drug treatment. The Lancet. 2019;393(10175):1034–44. DOI: 10.1016/S0140-6736(18)31808-7
48. Van Spall HGC, Lee SF, Xie F, Oz UE, Perez R, Mitoff PR et al. Effect of Patient-Centered Transitional Care Services on Clinical Outcomes in Patients Hospitalized for Heart Failure: The PACT-HF Randomized Clinical Trial. JAMA. 2019;321(8):753–61. DOI: 10.1001/jama.2019.0710
49. Laborde-Castérot H, Agrinier N, Zannad F, Mebazaa A, Rossignol P, Girerd N et al. Effectiveness of a multidisciplinary heart failure disease management programme on 1-year mortality: Prospective cohort study. Medicine. 2016;95(37):e4399. DOI: 10.1097/MD.0000000000004399
50. Vinogradova N.G. City Center for the Treatment of Chronic Heart Failure: the organiza-tion of work and the effectiveness of treatment of patients with chronic heart failure. Kardiologiia. 2019;59(2S):31–9. [Russian: Виноградова Н.Г. Городской центр лечения хронической сердечной недостаточности: организация работы и эффективность лечения пациентов с хронической сердечной недостаточностью. Кардиология. 2019;59(2S):31-9]. DOI: 10.18087/cardio.2621

ISSN 0022-9040. Kardiologiia. 2021;61(4). DOI: 10.18087/cardio.2021.4.n1628