Vinogradova N. G.[1, 2], Polyakov D. S.[1], Fomin I. V.[1]

[1] Privolzhsky Research Medical University, Nizhniy Novgorod, Russia

[2] Municipal Clinical Hospital #38 "Municipal Center for Treatment of Chronic Heart Failure", Nizhniy Novgorod, Russia

The risks of re-hospitalization of patients with heart failure with prolonged follow-up in a specialized center for the treatment of heart failure and in real clinical practice

Relevance	The number of patients with functional class III-IV chronic heart failure (CHF) characterized by frequent rehospitalization for acute decompensated HF (ADHF) has increased. Rehospitalizations significantly increase the cost of patient management and the burden on health care system.
Objective	To determine the effect of long-term follow-up at a specialized center for treatment of HF (Center for Treatment of Chronic Heart Failure, CTCHF) on the risk of rehospitalization for patients after ADHF.
Materials and Methods	The study successively included 942 patients with CHF after ADHF. Group 1 consisted of 510 patients who continued the outpatient follows-up at the CTCHF, and group 2 included 432 patients who refused of the follow-up at the CTCHF and were managed at outpatient clinics at their place of residence. CHF patient compliance with recommendations and frequency of rehospitalization for ADHF were determined by outpatient medical records and structured telephone calls. A rehospitalization for ADHF was recorded if the patient stayed for more than one day in the hospital and required intravenous loop diuretics. The follow-up period was two years. Statistical analyses were performed using a Statistica 7.0 software for Windows, SPSS, and a R statistical package.
Results	Patients of group 2 were significantly older, more frequently had FC III CHF and less frequently had FC I CHF than patients of group 1. Both groups contained more women and HF patients with preserved ejection fraction. Using the method of binary multifactorial logit-regression a mathematical model was created, which showed that risk of rehospitalization during the entire follow-up period did not depend on age and sex but was significantly increased 2.4 times for patients with FC III-IV CHF and 3.4 times for patients of group 2. Multinomial multifactorial logit-regression showed that the risk of one, two, three or more rehospitalizations within two years was significantly higher in group 2 than in group 1 (2.9–4.5 times depending on the number of rehospitalizations) and for patients with FC III-IV CHF compared to patients with FC I-II CHF (2–3.2 times depending on the number of rehospitalizations). Proportion of readmitted patients during the first year of follow-up was significantly greater in group 2 than in group 1 (55.3% vs. 39.8% of patients [odd ratio (OR) =1.9; 95% confidence interval (CI), 1.4–2.4; p<0.001]; during the second year, the proportion was 67.4% vs. 28.2% (OR=5.3; 95% CI, 3.9–7.1; p<0.001). Patients of group 1 were readmitted more frequently during the first year than during the second year (p<0,001) whereas patients of group 2 were readmitted more frequently during the second than the first year of follow-up (p<0.001). Total proportion of readmitted patients for two years of follow-up was significantly greater in group 2 (78.0% vs. 50.6%) (OR=3.5; 95% CI, 2.6–4.6; p<0.001). Reasons for rehospitalizations were identified in 88.7% and 45.9% of the total number of readmitted patients in groups 1 and 2, respectively. The main cause for ADHF was non-compliance with recommendations in 47.4% and 66.7% of patients of groups 1 and 2, respectively (p<0.001).
Conclusion	Follow-up in the system of specialized health care significantly decreases the risk of rehospitalization during the first and second years of follow-up and during two years in total for both patients with FC I-II CHF and FC III-IV CHF. Despite education of patients, personal contacts with medical personnel, and telephone support, main reasons for rehospitalization were avoidable.

Keywords	Repeated hospitalization; rehospitalization; Center for Treatment of Chronic Heart Failure; specialized medical care of patients with heart failure; chronic heart failure
For citation	Vinogradova N. G., Polyakov D. S., Fomin I. V. The risks of re-hospitalization of patients with heart failure with prolonged follow-up in a specialized center for the treatment of heart failure and in real clinical practice. Kardiologiia. 2020;60(3):59–69. [Russian: Виноградова Н. Г., Поляков Д. С., Фомин И. В. Риски повторной госпитализации пациентов с ХСН при длительном наблюдении в специализированном центре лечения ХСН и в реальной клинической практике. Кардиология. 2020;60(3):59–69.]

Corresponding author Vinogradova Nadezhda Georgievna. E-mail: vinogradovang@yandex.ru

As demonstrated by the EPOCH-CHF epidemiological study (Epidemiological Program: Chronic Heart failure), in the past 20 years the Russian Federation has seen an increase in the number of patients with chronic heart failure (CHF), which significantly increases the burden on the health care system [1]. The

increased prevalence of CHF is related to the improved survival rate of patients after myocardial infarction (MI), and the increased prevalence of hypertension, coronary artery disease (CAD), and diabetes mellitus (DM) [1–3].

It is well known that, from 1998 to 2014, the number of patients in the Russian Federation with CHF functional class (FC) III–IV characterized by frequent repeated decompensations and hospitalizations increased [1]. Repeated hospitalizations for acute decompensated heart failure (ADHF) increase the costs per patient and raise the risk of death within the first 30 days after discharge from the hospital [4–8].

According to the American Heart Association, more than half of all costs for the management of patients with CHF covered hospitalizations for CHF [9, 10]. In the United States and Europe, reducing the average occupancy rate and promoting early discharge were used to save on management costs for these patients. Unfortunately, a high rate of acute rehospitalizations was observed within 90 days after hospital discharge (21% of patients) [11, 12]. In another study, the rate of rehospitalizations within 30 days after discharge was 18%, almost half of which was due to the worsening of the CHF course [13]. In the European Society of Cardiology (ESC) – HF Pilot study, 43.9% of patients hospitalized with CHF were rehospitalized within 12 months [14].

According to the ESC and the Heart Failure Association of ESC, if a patient with CHF is hospitalized more than once in 6 months or more than twice in 12 months, then this patient is considered to be in an «advanced stage of CHF.» The algorithm of the inpatient management of such patients includes recommendations on education and inclusion of patients in a program of specialized follow-up before discharge from the hospital. According to the experts, early discharge after ADHF and prevention of subsequent rehospitalizations are only possible under these conditions [15].

The above data indicate high costs for health systems in different countries for the in-hospital treatment of CHF and the high rate of repeated hospitalizations. Experts from various countries estimate the costs for the management of patients with CHF as high, especially in the case of repeated hospitalization [6, 16–19]. The global community today devotes much attention to the creation of an effective model of special medical care to reduce the risk of repeated hospital admissions for patients with CHF [8, 15, 20–24].

This work analyzes the effectiveness of preventing repeated hospitalizations in patients after ADHF through long-term follow-up in a specialized CHF center (CHFC) in comparison with the standard management of patients in real-world outpatient practice.

Objective

Determine the effect of long-term follow-up in the specialized CHFC on the risks of repeated hospitalizations in patients after ADHF and determine risk factors (RFs) and immediate reasons for repeated hospitalizations.

Additional tasks were the following: Depict the clinical portrait of a modern patient with CHF after ADHF, identify factors determining the risk of repeated hospitalization, and explore the immediate reasons for deterioration of the clinical course of CHF and repeated hospitalization.

Materials and methods

The study was conducted in the specialized city CHFC (Nizhny Novgorod), that focuses on «seamless» specialized medical care for patients with CHF at the following stages: intensive care unit, inpatient department, outpatient department.

Within 12 months, 942 patients with CHF of any etiology (at age 18 years and above) were sequentially included in the prospective cohort study. They were treated for ADHF in the inpatient department of the CHFC. The patients were admitted in emergency due to the decompensation of at least one circulation circuit and the need for the intravenous administration of loop diuretics. All patients (or caregivers) were trained in the CHF patient school during the hospitalization and were advised at discharge to continue outpatient follow-up in the CHFC. During outpatient follow-up in the CHFC, cardiologist consultations were scheduled individually depending on the severity of the patient's condition, but not less than once in 3 months, supported by nursing control (structured telephone calls at least once a month). Thus, patients who continued follow-up in the outpatient department of the CHFC were under strict control, were regularly invited to revisit the center, and were in both face-to-face and phone contact with healthcare workers, which significantly improved compliance with CHF treatment. At outpatient visits and during phone calls, lifestyle, nutrition habits, low-sodium diet, discarding unhealthy habits, physical rehabilitation, and medications for CHF were discussed with patients. Patients who, after discharge, refused outpatient care in the CHFC, were followed up in local outpatient clinics, and were examined only over the phone by a CHFC nurse once a month within the first 12 months of follow-up, and then at least once every 3 months.

Patients were grouped depending on their decision to continue outpatient follow-up in the CHFC or at local outpatient clinics. Group 1 comprised 510 patients who were followed up in the CHFC within 2 years, and Group

ISSN 0022-9040. Kardiologiia. 2020;60(3). DOI: 10.18087/cardio.2020.3.n1002

2 included 432 patients who, after being discharged, refused follow-up in the CHFC and were supervised only in local outpatient clinics.

Patient compliance with the recommendations for the treatment of CHF and the rate of repeated hospitalizations for HF were assessed by outpatient records and structured phone calls. Analysis of data from outpatient records and structured phone calls were used to evaluate the direct reasons for repeated hospitalizations. Both at outpatient visits and during phone calls, patients answered questions about medications, implementing the recommendations for drug-free treatment, deterioration of comorbidities, and the onset of acute diseases just before the repeated hospitalization. All information, including low patient compliance, was registered in the medical records. In addition, analysis was carried out of the discharge summaries from the CHFC inpatient department. These contain full information on all acute and chronic CHF-related diseases and the immediate reasons for CHF deterioration in the «medical history» section. We classified the reasons for CHF deterioration and repeated hospitalizations as inevitable (i.e., objective reasons associated with chronic or acute CHF-related disease) or preventable (i.e., reasons related to violation by patients of the given recommendations). Violations of recommendations included diet violation, intake of high-sodium products and products contributing to fluid retention (e.g., a large quantity of watermelon or other melon), noncompliance with dosing, refusal to take some of the drugs, replacement of medications by some other medication, and refusal of medication.

Repeated hospitalization for the decompensation of CHF was taken into account if a patient spent more than 24 hours in the hospital and required the intravenous administration of loop diuretics. The follow-up period was 2 years.

Statistical analysis was performed using the Statistica 7.0 software package for Windows, SPSS, and the R software package. Data are presented as the mean and standard deviation (M, σ) with the parametric distribution of the sample. The Student's t-test was used with normal distribution, and the chi-squared test was used to analyze the rate differences. The Shapiro – Wilk test was used to verify the normality of distribution. If the distribution was different from normal, the Mann-Whitney test was used, and the nonparametric Wilcoxon test was used in the analysis of paired samples to assess the statistical significance of differences. When two groups were compared to assess the strength of an independent predictor variable's effect on the dependent variable (response), odds ratio (OR) and 95% confidence interval (CI) were determined. The methods of multivariate binary logit regression and multivariate multinomial logit regression were used to create mathematical models, in which a dependent variable and predictors were defined according to the parameters being analyzed. Differences were considered statistically significant with $p<0.05$.

Results

Table 1 shows the baseline clinical parameters of patients. Patients in Group 2 were significantly older. There were more female patients than male patients in both groups. The mean duration of in-hospital treatment for ADHF was 11 days in both groups. At discharge, patients did not differ in systolic (SBP) and diastolic (DBP) blood pressure or mean heart rate (Table 1).

In both groups, more patients with heart failure with preserved left ventricular ejection fraction (HFpEF) were observed. No statistically significant differences were observed in the rate of midrange EF (HFmrEF) and reduced EF (HFrEF) between the study groups (Table 1).

The 6 minute walk distance (6MWD) test was performed before discharge from the hospital, and Group 2 had worse results than Group 1. The same trend was observed when comparing the groups according to the Scale of Heart failure Optimizing Clinical Status (SHOCKS). The distribution of patients by CHF functional class (FC) showed that Group 2 included statistically significantly fewer patients with FC I and more patients with FC III CHF (Table 1).

The main reasons for CHF in the study groups were hypertension, chronic forms of CAD, history of MI, atrial fibrillation (AF), DM type 2, and acquired valvular heart disease (AVHD) of atherosclerotic origin. The rate of AVHDs was statistically significantly higher in Group 1 (Table 1).

Interestingly, the high comorbidity and polymorbidity of patients were observed, and there was a significant proportion of patients in both groups with peripheral atherosclerosis, chronic kidney disease, history of stroke, cancer, chronic obstructive pulmonary disease (COPD) and asthma, or pneumonia, respectively. The mean glomerular filtration rate (GFR) was statistically significantly lower in Group 2, but the proportion of patients with GFR less than 60 mL/min/1.73 m^2 was comparable between the groups. The total Charlson comorbidity index was estimated in both groups; the median was 5 points in both Group 1 and Group 2, without any statistically significant differences (Table 1).

Thus, Group 2 was characterized by a larger number of patients with FC III–IV CHF (56.9% vs. 47.1%, $p=0.002$), a lower mean 6MWD, and SHOKS 0–5 before discharge from the hospital. These facts were

Table 1. Baseline clinical parameters of patients in Group 1 and Group 2

Parameter	Group 1, n=510	Group 2, n=432	p*
Age, years	69.7 + 10.2	71.9 + 10.8	0.002
Male/female, % (n)	42.5 (217) / 57.5 (293)	41.4 (179) / 58.6 (253)	0.7
Duration of hospitalization, bed-days	11.4 + 3.1	11.3 + 3.4	0.95
SBP, mmHg	135.4 + 24.0	137.3 + 25.0	0.2
DBP, mmHg	77.3 + 12.1	78.7 + 13.1	0.1
SAD <120 mmHg, % (n)	19.8 (101)	18.3 (79)	0.6
HR, bpm	76.3 + 15.5	78 + 16.7	0.1
HFpEF / HFmrEF / HFrEF, % (n)	68.8 (351) / 17.9 (91) / 13.3 (68)	73.1 (316) / 17.6 (76) / 9.3 (40)	**0.1/0.9/0.05**
6MWD, m	299.2 + 102.1	276.3 + 94.2	**0.0003**
CHF FC I / II / III / IV, % (n)	13.9 (71) / 39 (199) / 38.6 (197) / 8.5 (43)	7.2 (31) / 35.9 (155) / 47 (203) / 9.9 (43)	0.0009/0.3/0.009/0.4
SHOKS, points	3 (Q1=2; Q3=4)	4 (Q1=2; Q3=5)	<0.001
History of hypertension, % (n)	94.5 (482)	95.3 (412)	0.5
History of CAD, % (n)	81.4 (415)	82.4 (356)	0.7
History of MI, % (n)	27.3 (139)	25.9 (112)	0.6
Peripheral atherosclerosis, % (n)	25.3 (129)	30.1 (130)	**0.1**
AVHD, % (n)	40.2 (205)	28.5 (123)	0.0002
History of DM/CI, % (n)	25.7 (131) / 10.4 (53)	23.8 (103) / 7.9 (34)	0.5 / 0.2
BMI, kg/m^2	30.1 + 6.6	31.0 + 10.7	0.3
Obesity, % (n)	47 (240)	38.7 (167)	0.3
AF, % (n)	49.8 (254)	44.0 (190)	**0.07**
GFR (CKD EPI) mL/min/1.73 m2	66.5 + 21.0	61.1 + 21.7	0.0003
GFR<60 mL/min/1.73 m^2, % (n)	35.5 (181)	40.5 (175)	0.1
History of CVA, % (n)	8.8 (45)	8.8 (38)	0.98
Anemia, % (n)	17.1 (87)	15.3 (66)	**0.5**
COPD, % (n)	15.7 (80)	10.4 (45)	**0.02**
Asthma, % (n)	5.1 (26)	2.5 (11)	0.044
Pneumonia during hospitalization, % (n)	7.1 (36)	9.9 (43)	0.1
History of cancer, % (n)	7.5 (38)	6.5 (28)	0.6
Charlson comorbidity index, points	5 (Q1=4; Q3=7)	5 (Q1=4; Q3=7)	0.6

*, the significance of differences between Group 1 and Group 2. BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HFpEF, heart failure with preserved left ventricular ejection fraction; HFmrEF, heart failure with midrange left ventricular ejection fraction; HFrEF, heart failure with reduced left ventricular ejection fraction; 6MWD, 6-minute walk distance; SHOKS, clinical assessment scale; CAD, coronary artery disease; MI, myocardial infarction; AVHD, acquired valvular heart disease; DM, diabetes mellitus; CI, carbohydrate intolerance; AF, atrial fibrillation; GFR, glomerular filtration rate; CVA, cerebrovascular accident; COPD, chronic obstructive pulmonary disease.

likely to contribute to the low mobility of patients and influenced their preferences to continue follow-up at local outpatient clinics.

An analysis of repeated hospitalizations over 2 years was made. During the follow-up period, the maximum number of repeated hospitalizations registered in one patient was seven within 2 years.

The proportion of rehospitalized patients during the first year of follow-up in Group 2 was statistically significantly higher in Group 1: 55.3% vs. 39.8% (OR 1.9, 95% CI: 1.4–2.4; p<0.001). The annual total mortality of patients statistically significantly differed between the groups: 4.2% in Group 1 and 14.4% in Group 2 (OR 3.9, 95% CI: 2.3–6.5; p<0.001). Among patients who were followed up for more than 1 year, the proportion of rehospitalized patients during the second year of follow-up was higher in Group 2 (67.4% vs. 28.2%, OR 5.3, 95% CI: 3.9–7.1; p<0.001).

Group 1 patients were rehospitalized more often in the first year of follow-up (39.8%) than in the second year (28.2%), p<0.001. In Group 2, by contrast, the repeated hospitalizations were more frequent (67.4%) in the second year of follow-up than in the first year (55.3%), p<0.001.

The total number of rehospitalized patients within 2 years of follow-up in Group 2 was statistically significantly higher (78.0% vs. 50.6%) (OR 3.5, 95% CI: 2.6–4.6; p<0.001).

Given that Group 2 included significantly more patients with FC III CHF than Group 1, we divided patients

ISSN 0022-9040. Kardiologiia. 2020;60(3). DOI: 10.18087/cardio.2020.3.n1002

Table 2. Proportion of rehospitalized patients within 2 years of follow-up by groups and CHF FCs

Group	FC I-II	FC III-IV	p*
Group 1	40.7%	61.7%	<0.001
Group 2	69.9%	84.1%	0.0004
$p_{1/2}$**	<0.001	<0.001	

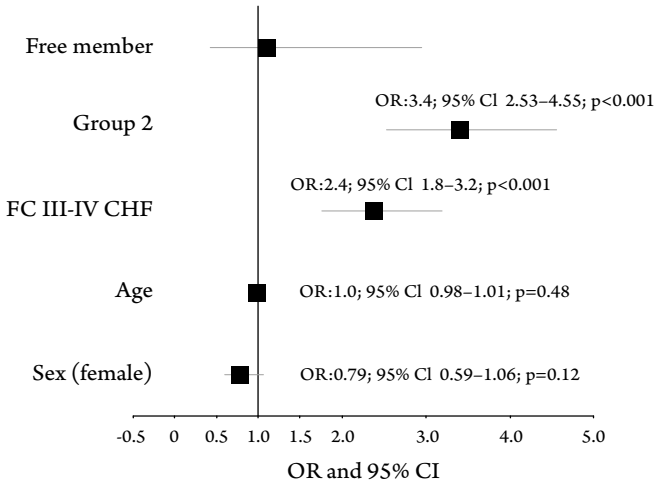
*, the significance of differences within Groups 1 and Group 2 between FC I–II and FC III–IV; **, the significance of differences between Group 1 and Group 2. FC, functional class.

Table 3. The risk of repeated hospitalization within two years according to the multivariate analysis

Variable	OR	95% CI	p
Group 2	3.4	2.53–4.55	<0.001
FC III-IV CHF	2.40	1.80–3.20	<0.001
Age	1.00	0.98–1.01	0.48
Female	0.79	0.59–1.06	0.12

OR, odds ratio; CI, confidene interval;
FC, functional class; CHF, congestive heart failure.

Figure 1. Risk of repeated hospitalization within 2 years by follow-up group, CHF FC, age, and sex of patients, according to the multivariate analysis



in both groups into subgroups of FC I–II and FC III–IV CHF. We defined the repeated hospitalization in these subgroups. The data are given in Table 2.

In both groups, patients with FC III–IV were rehospitalized more often than patients with FC I–II CHF. The comparison of patients with FC I–II showed that patients in Group 2 were rehospitalized more often. The same trend was found when patients with FC III–IV were compared between Group 1 and Group 2 (Table 2).

Using the method of multivariate binary logit regression, we created a mathematical model in which the following variables were used: follow-up of patients in Group 2, presence of FC III–IV CHF, age, and female sex (Table 3, Figure 1).

Age and sex did not have a statistically significant effect on the risk of repeated hospitalization within 2 years. The risk of repeated hospitalization was insignificantly lower in female patients. The presence of FC III–IV CHF and the fact of follow-up in Group 2 were statistically significant independent predictors of repeated hospitalization. The presence of FC III–IV CHF increased the risk of repeated hospitalization 2.4 times, and follow-up in Group 2 increased this risk 3.4 times, within 2 years (Table 3, Figure 1).

We analyzed the probability and number of repeated hospitalizations according to groups and CHF FCs within 2 years of follow-up using multivariate analysis (Figure 2).

The number of rehospitalizations per patient within 2 years of follow-up ranged from 0 to 7. Patients were divided into subgroups according to a CHF FC. Most patients with FC I–II CHF in Group 1 were not hospitalized again or were rehospitalized once or twice; patients with FC III–IV CHF in Group 1 as expected were rehospitalized more times. Regardless of the baseline CHF FC, Group 2, by contrast, is characterized by a high probability of repeated hospitalization within 2 years of follow-up (Figure 2).

To make the probability data and the number of repeated hospitalizations (Figure 2) meaningful, the «number of hospitalizations» variable was transformed into a qualitative variable with the following gradations: «no rehospitalizations,» «one rehospitalization,» «two rehospitalizations,» «three or more rehospitalizations» (data are given in Figure 3).

Taking into account the above gradations of rehospitalizations, we performed an analysis using the method of multinominal logit regression; results are given in Table 4 and Figure 4.

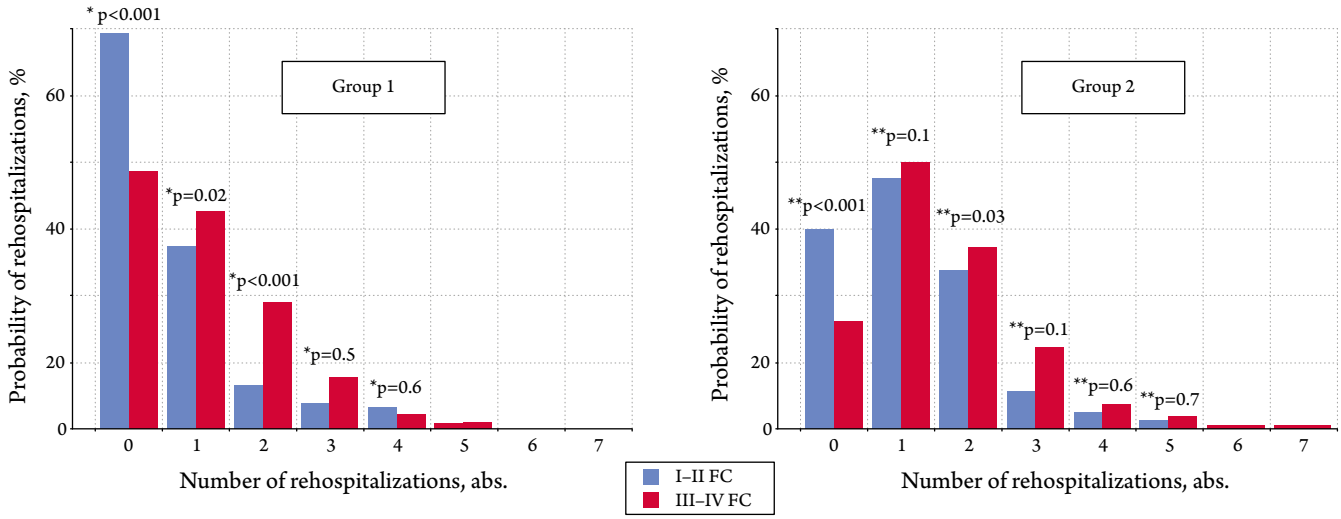
The risk of one, two, three, or more repeated hospital admissions within 2 years was statistically significantly higher in Group 2 than in Group 1 (2.9–4.5 times, depending on the number of hospitalizations) and in FC III–IV CHF than in FC I–II CHF (2–3.2 times higher, depending on the number of admissions) in both groups (Table 4; Figure 4).

Age did not increase the risk of one, two, three, or more hospitalizations, and female sex insignificantly reduced this risk (Table 4; Figure 4).

We analyzed the immediate reasons for development of repeated ADHF and hospitalizations for HF in patients of the two study groups (Figure 5).

Reasons for the repeated hospitalizations are identified in 88.7% of cases in the total number of rehospitalized patients in Group 1, and in 45.9% in Group 2. The structure of the reasons for ADHF is provided for

Figure 2. Probability and number of repeated hospitalizations by group and CHF FC, according to the multivariate analysis



** The calculation of the p value between Group 1 and Group 2 is given for FC I-II CHF and matching probabilities by the number of rehospitalizations. ** The calculation of the p value between Group 1 and Group 2 is given for FC III-IV CHF and matching probabilities by the number of rehospitalizations. CHF – Congestive Heart Failure; FC- functional class.*

rehospitalized patients with known immediate reasons for DHF.

Hypertensive crisis was not a common reason for ADHF and repeated hospitalization in the study group patients. The deterioration of the clinical course of CAD as the reason for ADHF was reported more often than either hypertensive crisis or cardiac arrhythmias. Pneumonia as the main reason for ADHF was reported in both groups, and infections (acute respiratory diseases) only in Group 1. Aggravation of chronic obstructive pulmonary disease (COPD) and asthma and suboptimal treatment of these diseases were the immediate reasons for ADHF only in Group 1. Anemia was also the reason for ADHF only in Group 1 (Figure 5).

The reasons mentioned above for ADHF were inevitable. However, preventable reasons were also identified in study group patients. We classified them as «noncompliance with the recommendations.» Noncompliance with the recommendations as the reason for ADHF was detected in 47.4% of patients in Group 1 and 66.7% of patients in Group 2 (p<0.001) (Figure 5).

Table 4. Risk rehospitalization according to group, CHF FC, age, and sex

Variable	OR	95% CI	p
One rehospitalization			
Group 2	2.91	2.10–4.04	<0.001
FC III-IV CHF	2.03	1.47–2.81	<0.001
Age	0.99	0.97–1.01	0.21
Female	0.84	0.60–1.16	0.29
Two rehospitalizations			
Group 2	4.53	3.05–6.76	<0.001
FC III-IV CHF	2.83	1.89–4.22	<0.001
Age	1.00	0.99–1.03	0.54
Female	0.73	0.49–1.09	0.12
Three or more rehospitalizations			
Group 2	3.48	2.18–5.54	<0.001
FC III-IV CHF	3.19	1.98–5.15	<0.001
Age	0.99	0.97–1.02	0.58
Female	0.76	0.47–1.21	0.25

CHF, congestive heart failure;
FC, functional class; OR, odds ratio; CI, confidence interval.

Discussion

In our study, Group 1 patients were enrolled in a system of specialized medical care, including cardiological consultations and phone-call nursing support, which significantly influenced the patients' compliance with the treatment. Patients in Group 2 refused outpatient follow-up in the specialized CHFC but could be hospitalized again in the inpatient department of the CHFC.

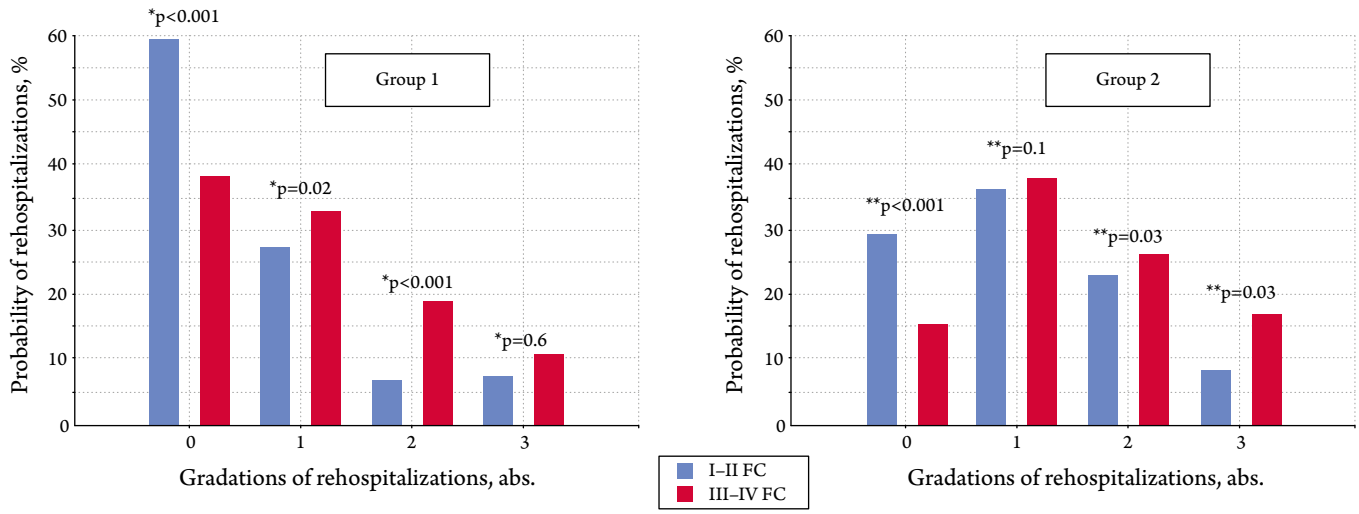
Patients in Group 2 were statistically significantly older, which could affect their decision to continue follow-up at a local outpatient clinic. Noncompliance with the follow-up in the specialized CHFC might also be caused by the severity of the patient's condition, because the mean value of 6MWD was lower, the SHOKS score was higher, and FC III CHF was statistically significantly more common in Group 2.

Interestingly, there were more female patients in both groups, and there were no statistically significant differences by sex between the study groups.

The patient's age was not a predictor of repeated hospitalization due to the deterioration of HF or a factor increasing the number of admissions per patient.

ISSN 0022-9040. Kardiologiia. 2020;60(3). DOI: 10.18087/cardio.2020.3.n1002

Figure 3. Probability of repeated hospitalizations depending on gradation, Group 1 and Group 2



0—no rehospitalizations; 1—one rehospitalization; 2—two rehospitalizations; 3—three or more rehospitalizations. CHF – Congestive Heart Failure; FC- functional class.
** The calculation of the p value between Group 1 and Group 2 is given for FC I-II CHF and matching probabilities by the number of rehospitalizations.*
*** The calculation of the p value between Group 1 and Group 2 is given for FC III-IV CHF and matching probabilities by the number of rehospitalizations.*

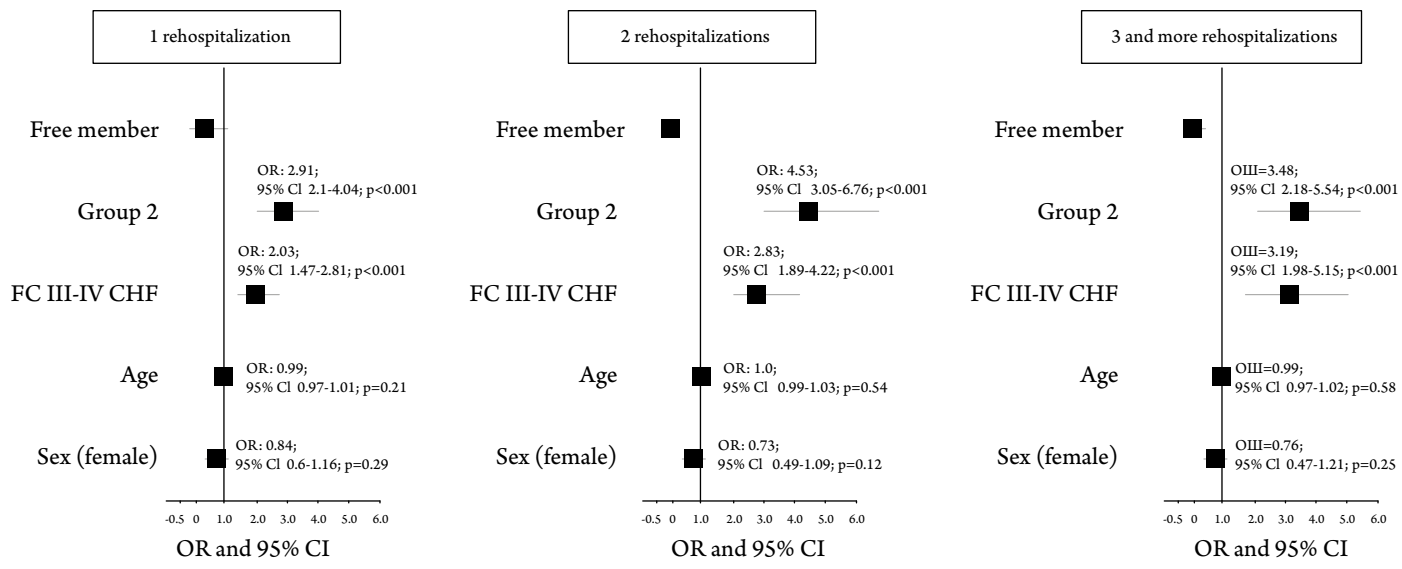
Distribution by LVEF showed that in our study HFpEF was registered more often among patients after ADHF, in both groups. According to the EPOCH-CHF study, preserved LVEF was also identified in more than half of patients with CHF in the sample of the European Russian population [26], and HFpEF was registered in 84.1% of patients in the Russian sample of the IMPROVEMENT HF study [27]. The predominance of HFpEF is thereby common in both outpatients and hospitalized patients with CHF in the Russian Federation.

The main etiologies for CHF in the study groups were hypertension, chronic forms of CAD, history of MI, AF, DM type 2, AVHD of atherosclerotic origin. This structure of reasons for CHF characteristics in European Russia was demonstrated previously in the EPOCH and EPOCH-D–CHF studies [28, 29].

Our findings showed that the proportion of re-hospitalized patients within the first and second years and in both years combined was higher in Group 2. Interestingly, the rate of hospitalizations was higher in the first year of follow-up in Group 1, and in the second year of follow-up in Group 2.

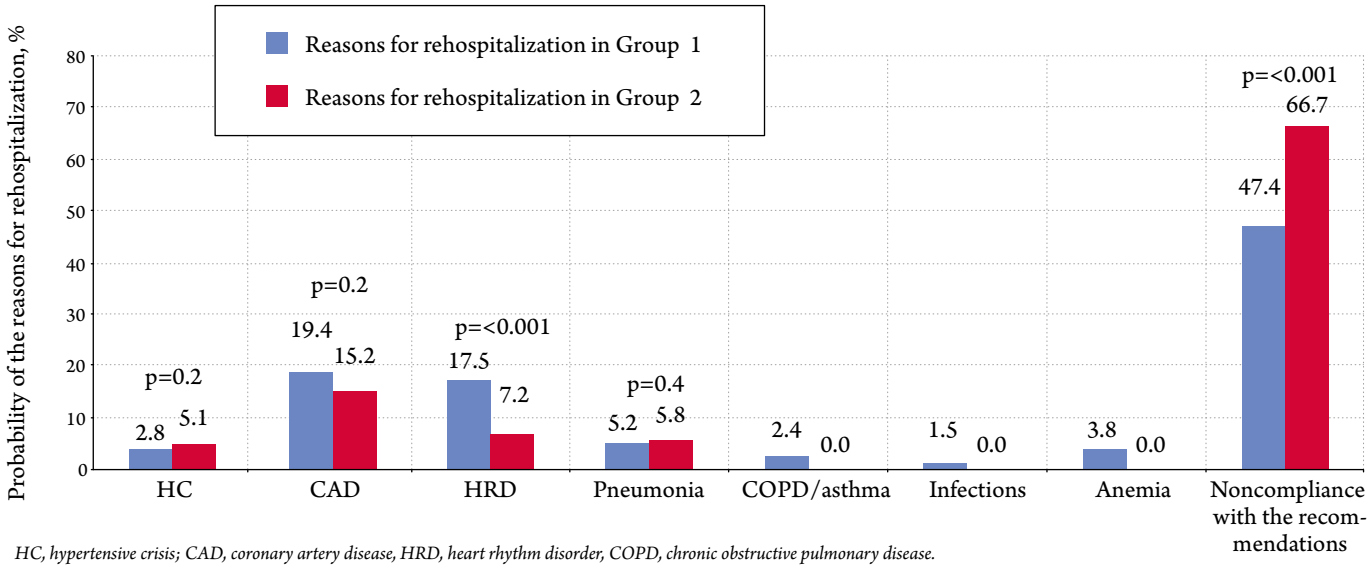
It should be noted that patients in Group 1, who were in regular contact with healthcare workers at the CHFC, were hospitalized in priority by referral from a cardiologist of the outpatient department of the CHFC. Within the first year after ADHF, CHF probably was compensated in

Figure 4. Risk rehospitalization by group, CHF FC, age, and sex



CHF – Congestive Heart Failure; FC- functional class; OR – Odds Ratio; CI – Confident interval

Figure 5. Immediate reasons for ADHF in case of repeated hospitalization of patients, Groups 1 and Group 2



HC, hypertensive crisis; CAD, coronary artery disease, HRD, heart rhythm disorder, COPD, chronic obstructive pulmonary disease.

some patients of Group 1, or there were factors adversely affecting the clinical course of CHF, which required repeated hospitalizations. Patients in Group 1 were informed about symptoms of CHF decompensation, in case of which they were to call an ambulance for emergency hospitalization. In Group 1, the decrease in the number of patients rehospitalized in the second year of follow-up shows the stabilization of CHF.

In Group 2, the probability of survival of patients until the second year of the study was lower than that in Group 1, which may be associated with a lower rate of repeated hospitalizations within the first year of follow-up. According to the structured phone calls, Group 2 was characterized by a more significant number of patients who was not compliant with HF medication and had marked symptoms of CHF but did not seek medical care. If rehospitalizations in Group 2 were more frequent within the first year of follow-up, the survival of patients might have been higher.

It is important to note that there were more patients with FC III CHF in Group 2 than in Group 1. The distribution of patients of both groups into subgroups by CHF FC showed that patients with FC III–IV CHF in both groups were hospitalized statistically significantly more often within 2 years of follow-up. We compared the proportion of rehospitalized patients with FC I–II and FC III–IV between Group 1 and Group 2, and found a statistically significant increase in the proportion of rehospitalized patients in Group 2 as compared with Group 1 within 2 years of follow-up.

Analysis of data of the multivariate binary and multinominal logit regression revealed that the risk of repeated hospitalization increases significantly in the presence of FC III–IV CHF and when patients are followed up in local nonspecialized outpatient facilities (Group 2).

We were able to identify the immediate reasons for the deterioration of CHF and repeat hospitalizations for a portion of patients (88.7% in Group 1 and 45.9% in Group 2). Unfortunately, the reasons for hospitalizations of about half of patients in Group 1 and the majority of patients in Group 2 were preventable, which were classified as «noncompliance with the recommendations.»

This fact proves that, in this cohort of older and polymorbid patients, it is challenging to modify lifestyle and dietary habits and sometimes maintain compliance with multicomponent and often expensive drug therapy of CHF. It is thereby essential to launch CHF patient schools in all outpatient facilities and develop CHF treatment reimbursement programs.

Hypertensive crisis does not seem to be a common and relevant reason for the development of ADHF, because, on the one hand, modern cardiology administers more sustained-release antihypertensive agents [3], and, on the other hand, patients with CHF often have hypotension in ADHF [30].

In general, it should be noted that ADHF and the immediate period after its relief and discharge from hospital are a vulnerable period for the patient, in which he/she can develop hypotension, deterioration of renal function, and other complications, increasing the risk of death. During this period, it is important to evaluate organ damage and make every effort to properly titrate the drug therapy, taking into account the patient's characteristics, which could allow a patient to overcome

ISSN 0022-9040. Kardiologiia. 2020;60(3). DOI: 10.18087/cardio.2020.3.n1002

this vulnerable period safely. The administration of sacubitril/valsartan is of interest in ADHF and before discharge as the basis of optimal drug therapy in patients with systolic dysfunction. Reliable data were obtained, showing not only improved prognosis but also the effective prevention of repeated hospitalizations in the immediate period after discharge as compared with ACEIs [31, 32].

Healthcare professionals should see the repeated hospitalizations of patients with CHF as high material costs, and ADHF as the most vulnerable period for the disease to worsen the structural and functional state of the myocardium and the general prognosis for a patient. Thus, the «seamless» model of medical care for patients after discharge seems to be the best possible, and drug therapy aimed at reducing the probability of rehospitalizations should be recommended in this category of patients.

Our findings show the high effectiveness of prevention of repeated hospitalizations after ADHF when patients are enrolled in the system of «seamless» specialized medical care. Previous studies also confirm that the prevention of repeated hospitalizations in the immediate and long-term periods was accomplished in patients involved in the programs of specialized medical care in CHF [33–36].

These programs involved the participation of interdisciplinary teams and programs of follow-up by cardiologists or physicians specializing in CHF, or by nurses [36–38].

Conclusions

1. The modern portrait of the patient after ADHF is characterized by a higher proportion of female patients and patients with HFpEF, as well as high comorbidity and polymorbidity.
2. Age and sex do not affect the risk of repeated hospitalization, and FC III–IV CHF increases the risk of repeated hospital admission.
3. Specialized medical follow-up, as demonstrated by the city CHFC, reduces the risks of repeated hospitalization during the first and second 12 months of follow-up and within 2 years in total in patients both with FC I–II and FC III–IV CHF.
4. Despite the education of patients, personal contact with the healthcare workers (CHFC group), and phone-call support, the main reasons for repeated hospitalization were preventable.

No conflict of interest is reported.

The article was received on 15/01/20

REFERENCES

1. 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
2. Dedov I.I., Shestakova M.V., Vikulova O.K. Epidemiology of diabetes mellitus in Russian Federation: clinical and statistical report according to the federal diabetes registry. Diabetes mellitus. 2017;20(1):13–41. [Russian: Дедов И.И., Шестакова М В., Викулова О К. Эпидемиология сахарного диабета в Российской Федерации: клинико-статистический анализ по данным Федерального регистра сахарного диабета. Сахарный диабет. 2017;20(1):13–41]. DOI: 10.14341/DM8664
3. Badin Yu.V., Fomin I.V., Belenkov Yu.N., Mareev V.Yu., Ageev F.T., Polyakov D.S. et al. EPOCHA-AH 1998–2017. Dynamics of prevalence, awareness of arterial hypertension, treatment coverage, and effective control of blood pressure in the European part of the Russian Federation. Kardiologiia. 2019;59(1S):34–42. [Russian: Бадин Ю.В., Фомин И.В., Беленков Ю.Н., Мареев В.Ю., Агеев Ф.Т., Поляков Д.С. и др. ЭПОХА-АГ 1998–2017 гг.: Динамика распространенности, информированности об артериальной гипертонии, охвате терапией и эффективного контроля артериального давления в Европейской части РФ. Кардиология. 2019;59(1S):34-42]. DOI: 10.18087/cardio.2445
4. 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
5. Setoguchi S, Stevenson LW, Schneeweiss S. Repeated hospitalizations predict mortality in the community population with heart failure. American Heart Journal. 2007;154(2):260–6. DOI: 10.1016/j.ahj.2007.01.041
6. Correction to "Rehospitalization in a National Population of Home Health Care Patients with Heart Failure". Health Services Research. 2017;52(5):1958–60. DOI: 10.1111/1475-6773.12761
7. Okumura N, Jhund PS, Gong J, Lefkowitz MP, Rizkala AR, Rouleau JL et al. Importance of Clinical Worsening of Heart Failure Treated in the Outpatient Setting: Evidence From the Prospective Comparison of ARNI With ACEI to Determine Impact on Global Mortality and Morbidity in Heart Failure Trial (PARADIGM-HF). Circulation. 2016;133(23):2254–62. DOI: 10.1161/CIRCULATIONAHA.115.020729
8. Desai AS, Stevenson LW. Rehospitalization for Heart Failure: Predict or Prevent? Circulation. 2012;126(4):501–6. DOI: 10.1161/CIRCULATIONAHA.112.125435
9. Lloyd-Jones D, Adams RJ, Brown TM, Carnethon M, Dai S, De Simone G et al. Executive Summary: Heart Disease and Stroke Statistics -2010 Update: A Report from the American Heart Association. Circulation. 2010;121(7):948–54. DOI: 10.1161/CIRCULATIONAHA.109.192666
10. Blecker S, Paul M, Taksler G, Ogedegbe G, Katz S. Heart failure–associated hospitalizations in the United States. Journal of the American College of Cardiology. 2013;61(12):1259–67. DOI: 10.1016/j.jacc.2012.12.038
11. Ambrosy AP, Fonarow GC, Butler J, Chioncel O, Greene SJ, Vaduganathan M et al. The Global Health and Economic Burden

of Hospitalizations for Heart Failure. Journal of the American College of Cardiology. 2014;63(12):1123–33. DOI: 10.1016/j.jacc.2013.11.053
12. Storrow AB, Jenkins CA, Self WH, Alexander PT, Barrett TW, Han JH et al. The Burden of Acute Heart Failure on U.S. Emergency Departments. JACC: Heart Failure. 2014;2(3):269–77. DOI: 10.1016/j.jchf.2014.01.006
13. Carson PE, Anand IS, Win S, Rector T, Haass M, Lopez-Sendon J et al. The Hospitalization Burden and Post-Hospitalization Mortality Risk in Heart Failure with Preserved Ejection Fraction. JACC: Heart Failure. 2015;3(6):429–41. DOI: 10.1016/j.jchf.2014.12.017
14. Maggioni AP, Dahlström U, Filippatos G, Chioncel O, Crespo Leiro M, Drozdz J et al. EURObservational Research Programme: regional differences and 1-year follow-up results of the Heart Failure Pilot Survey (ESC-HF Pilot). European Journal of Heart Failure. 2013;15(7):808–17. DOI: 10.1093/eurjhf/hft050
15. 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
16. Heidenreich PA, Albert NM, Allen LA, Bluemke DA, Butler J, Fonarow GC et al. Forecasting the Impact of Heart Failure in the United States: A Policy Statement from the American Heart Association. Circulation: Heart Failure. 2013;6(3):606–19. DOI: 10.1161/HHF.0b013e318291329a
17. 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
18. Bello NA, Claggett B, Desai AS, McMurray JJV, Granger CB, Yusuf S et al. Influence of Previous Heart Failure Hospitalization on Cardiovascular Events in Patients with Reduced and Preserved Ejection Fraction. Circulation: Heart Failure. 2014;7(4):590–5. DOI: 10.1161/CIRCHEARTFAILURE.113.001281
19. Shafie AA, Tan YP, Ng CH. Systematic review of economic burden of heart failure. Heart Failure Reviews. 2018;23(1):131–45. DOI: 10.1007/s10741-017-9661-0
20. Zannad F. Rising incidence of heart failure demands action. The Lancet. 2018;391(10120):518–9. DOI: 10.1016/S0140-6736(17)32873-8
21. 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
22. Conrad N, Judge A, Tran J, Mohseni H, Hedgecott D, Crespillo AP et al. Temporal trends and patterns in heart failure incidence: a population-based study of 4 million individuals. The Lancet. 2018;391(10120):572–80. DOI: 10.1016/S0140-6736(17)32520-5
23. Stewart S, Carrington MJ, Marwick T, Davidson PM, Macdonald P, Horowitz J et al. The WHICH? trial: rationale and design of a pragmatic randomized, multicentre comparison of home- vs. clinic-based management of chronic heart failure patients. European Journal of Heart Failure. 2011;13(8):909–16. DOI: 10.1093/eurjhf/hfr048
24. Grady KL, Dracup K, Kennedy G, Moser DK, Piano M, Stevenson LW et al. Team Management of Patients with Heart Failure: A Statement for Healthcare Professionals from the Cardiovascular Nursing Council of the American Heart Association. Circulation. 2000;102(19):2443–56. DOI: 10.1161/01.CIR.102.19.2443
25. R Core Team (2018). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. 2018. [Internet] 2018. Available at: https://www.r-project.org/
26. Mareev V.Yu., Danielyan M.O., Belenkov Yu.N. Comparative characteristics of patients with CHF in relation to the value of injection fraction by data from the Russian multicenter study EPOCH-A-CHF: once more about the problem of CHF with preserved left ventricular systolic function. Russian Heart Failure Journal. 2006;7(4):164–71. [Russian: Мареев В.Ю., Даниелян М.О., Беленков Ю.Н. Сравнительная характеристика больных с ХСН в зависимости от величины ФВ по результатам Российского многоцентрового исследования ЭПОХА-О-ХСН: снова о проблеме ХСН с сохраненной систолической функцией левого желудочка. Журнал Сердечная Недостаточность. 2006;7(4):164- 71]
27. Belenkov Yu.N., Mareev V.Yu. How do we diagnose and treat heart failure in real clinical practice in the early 21st century? The results of the study IMPROVEMENT HF. Consilium Medicum. 2001;3(2):65–73. [Russian: Беленков Ю.Н., Мареев В.Ю. Как мы диагностируем и лечим сердечную недостаточность в реальной клинической практике в начале XXI века? Результаты исследования IMPROVEMENT HF. Consilium Medicum. 2001; 3(2):65-73]
28. Fomin I.V. Epidemiology of chronic heart failure in the Russian Federation. In: Chronic heart failure-M.: GEOTAR-Media;2010. [Russian: Фомин И. В. Эпидемиология хронической сердечной недостаточности в Российской Федерации. В: Хроническая сердечная недостаточность. – М.: ГЭОТАР-Медиа; 2010. – С. 7–77]
29. Polyakov D.S., Fomin I.V., Valikulova F.Yu., Vaisberg A.R., Kraiem N., Badin Yu.V. et al. The EPOCHA-CHF epidemiological program: decompensated chronic heart failure in real-life clinical practice (EPOCHA-D-CHF). Russian Heart Failure Journal. 2016;17(5):299–305. [Russian: Поляков Д.С., Фомин И.В., Валикулова Ф.Ю., Вайсберг А.Р., Краием Н., Бадин Ю.В. и др. Эпидемиологическая программа ЭПОХА–ХСН: Декомпенсация хронической сердечной недостаточности в реальной клинической практике (ЭПОХА–Д–ХСН). Журнал Сердечная Недостаточность. 2016;17(5):299–305]. DOI: 10.18087/rhfj.2016.5.2239
30. Polyakov D.S., Fomin I.V., Badin Yu.V., Vaisberg A.R., Valikulova F.Yu., Shechrbinina E.V. et al. Effects of systolic and diastolic blood pressure and its changes between successive hospitalizations on prognosis for patients with acute decompensated CHF. Russian Heart Failure Journal. 2017;18(3):178–84. [Russian: Поляков Д.С., Фомин И.В., Бадин Ю.В., Вайсберг А.Р., Валикулова Ф.Ю. Щербинина Е.В. и др. Влияние уровня систолического и диастолического артериального давления и его динамики между последовательными госпитализациями на прогноз пациента с ХСН при острой декомпенсации. Журнал Сердечная Недостаточность. 2017;18(3):178-84]. DOI: 10.18087/rhfj.2017.3.2357
31. Velazquez EJ, Morrow DA, DeVore AD, Duffy CI, Ambrosy AP, McCague K et al. Angiotensin–Neprilysin Inhibition in Acute Decompensated Heart Failure. New England Journal of Medicine. 2019;380(6):539–48. DOI: 10.1056/NEJMoa1812851
32. McMurray JJV, Packer M, Desai AS, Gong J, Lefkowitz MP, Rizkala AR et al. Dual angiotensin receptor and neprilysin inhibition as an alternative to angiotensin-converting enzyme inhibition in patients with chronic systolic heart failure: rationale for and design of the 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. 2013;15(9):1062–73. DOI: 10.1093/eurjhf/hft052
33. Chang S, Davidson PM, Newton PJ, Macdonald P, Carrington MJ, Marwick TH et al. Composite outcome measures in a pragmatic clinical trial of chronic heart failure management:

ISSN 0022-9040. Kardiologiia. 2020;60(3). DOI: 10.18087/cardio.2020.3.n1002

A comparative assessment. International Journal of Cardiology. 2015; 185:62–8. DOI: 10.1016/j.ijcard.2015.03.071
34. Von Scheidt W, Zugck C, Pauschinger M, Hambrecht R, Bruder O, Hartmann A et al. Characteristics, management modalities and outcome in chronic systolic heart failure patients treated in tertiary care centers: results from the EVIdence based TreAtment in Heart Failure (EVITA-HF) registry. Clinical Research in Cardiology. 2014;103(12):1006–14. DOI: 10.1007/s00392-014-0743-x
35. McAlister FA, Stewart S, Ferrua S, McMurray JJJV. Multidisciplinary strategies for the management of heart failure patients at high risk for admission. Journal of the American College of Cardiology. 2004;44(4):810–9. DOI: 10.1016/j.jacc.2004.05.055
36. Sochalski J, Jaarsma T, Krumholz HM, Laramee A, McMurray JJV, Naylor MD et al. What Works In Chronic Care Management: The Case Of Heart Failure. Health Affairs. 2009;28(1):179–89. DOI: 10.1377/hlthaff.28.1.179
37. Stewart S, Horowitz JD. Specialist Nurse Management Programmes: Economic Benefits in the Management of Heart Failure. PharmacoEconomics. 2003;21(4):225–40. DOI: 10.2165/00019053-200321040-00001
38. Strömberg A, Mårtensson J, Fridlund B, Levin L-A, Karlsson J-E, Dahlström U. Nurse-led heart failure clinics improve survival and self-care behaviour in patients with heart failure: results from a prospective, randomised trial. European Heart Journal. 2003;24(11):1014–23. DOI: 10.1016/S0195-668X(03)00112-X