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Prognostic value of atrial fibrillation in patients with heart failure and different left ventricular ejection fraction: results of the multicenter RIF-CHF register

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Heart failure (HF) and atrial fibrillation (AF) are the most common cardiovascular conditions in clinical practice and frequently coexist. The number of patients with HF and AF is increasing every year.

Aim. To analyze the effect of clinical course and management of HF and AF on the outcomes.

Material and methods. The data of 1003 patients from the first Russian register of patients with HF and AF (RIF-CHF) were analyzed. The endpoints included hospitalization due to decompensated HF, cardiovascular mortality, thromboembolic events, and major bleeding. Predictors of unfavorable outcomes were analyzed separately for patients with HF with preserved ejection fraction (AF+HFpEF), mid-range ejection fraction (AF+HFmrEF), and reduced ejection fraction (AF+HFrEF).

Results. Among all patients with HF, 39% had HFpEF, 15% — HFmrEF, and 46% — HFrEF. A total of 57,2% of patients were rehospitalized due to decompensated HF within one year. Hospitalization risk was the highest for HFmrEF patients (66%, p=0,017). Reduced ejection fraction was associated with the increased risk of cardiovascular mortality (15,5% vs 5,4% in other groups, p<0,001) but not ischemic stroke (2,4% vs 3%, p=0,776). Patients with HFpEF had lower risk to achieve the composite endpoint (stroke+MI+cardiovascular death) as compared to patients with HFmrEF and HFrEF (12,7% vs 22% and 25,5%, p<0,001). Regression logistic analysis revealed that factors such as demographic characteristics, disease severity, and selected therapy had different effects on the risk of unfavorable outcomes depending on ejection fraction group.

Conclusion. Each group of patients with different ejection fractions is characterized by its own pattern of factors associated with unfavorable outcomes. The demographic and clinical characteristics of patients with mid-range ejection fraction demonstrate that these patients need to be studied as a separate cohort.

Key words: heart failure, atrial fibrillation, left ventricular ejection fraction, treatment.

Relationships and Activities: none.

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The incidence of heart failure (HF) and atrial fibrillation (AF) in the world has the pandemic character [1]. This is largely due to population ageing and improvement in survival rate of patients with cardiovascular diseases [2]. According to epidemiological studies, >37 million people worldwide suffer from AF [3]. According to the Framingham study, the risk of developing AF in people over 55 years of age is 37% [4]. AF not only reduces the quality of life, but also worsens the prognosis. The 10-year survival rate among people with AF aged 55 to 74 years is 42,4% and 38,5% for women and men, compared to 79,1% and 70% for women and men without AF [5].

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Worldwide, >64 million people suffer from chronic HF (CHF) [3]. Population-based studies show that the CHF incidence is higher among men than among women, and increases dramatically with age [6]. The CHF prevalence among the population of developed countries is 1-3%, increasing to 10% and 30% in the age groups over 70 and 85 years, respectively [7]. In comparison with the increase in the AF incidence over the past few decades, the number of new cases of HF during this period was stable. The increase in the number of patients with CHF is largely associated with improved survival rate [8, 9].

CHF and AF are often combined with each other. This can be partly explained by the presence of common risk factors (RF), such as age, hypertension, coronary heart disease, diabetes mellitus, obesity, obstructive sleep apnea syndrome, valvular disease, kidney disease, smoking [10, 11]. HF develops in two-thirds of people with AF, and AF, in turn, complicates the HF course in one-third of patients [12, 13]. The combination of CHF and AF increases the stroke risk, admission due to CHF decompensation and overall mortality rate [14]. According to the Framingham study, mortality rates (per 1000 patient-years) in patients with HF and the development of new AF were 257 and 302 for patients with HF with preserved ejection fraction (EF) (HFpEF) and HF with reduced EF (HFrEF), respectively, compared with 120 in patients without HF. Mortality rate (per 1000 patient-years) in patients with a new diagnosis of HF and previous AF was 290 compared to 244 in people without AF [12]. As the RE-LY study analysis has shown, HF is an independent predictor of overall mortality rate and has the highest predictive significance for cardiovascular mortality in patients with AF [15]. An additional point is that unlike patients with sinus rhythm, patients with HFrEF and concomitant AF have no effect from beta-blocker therapy from viewpoint of overall mortality rate, mortality rate from cardiovascular diseases, or hospitalization [16]. This highlights the importance of analyzing the outcomes of patients with CHF in AF, rather than extrapolating data from patients with sinus rhythm.

According to the European Guidelines for HF management (2016), HF is divided into 3 clinical subtypes: HFpEF: EF ⩾50%, HF with midrange EF (HFmrEF): 40⩽ EF <49% and HFrEF: EF <40% [17]. These groups of patients have major differences in a number of parameters, ranging from epidemiology, etiology and pathogenesis to diagnosis, therapeutic strategy and prognosis. Many questions on the therapeutic strategy remain to be resolved. One reason is that our HFpEF and HFmrEF knowledge is limited to data from retrospective studies or subanalyses of randomized trials [17, 18].

Our study was aimed at analyzing the features of the CHF course in combination with AF, collecting data on diagnosis, treatment and level of compliance with clinical recommendations for CHF and AF treatment in the Russian Federation.

Material and methods

The study design was described earlier [19]. A multicenter prospective observational study from February 2015 to January 2016 enrolled 1003 patients with CHF in combination with AF. The patients were enrolled in 30 medical centers from 21 regions of the Russian Federation. All patients had a confirmed diagnosis of CHF and AF, in accordance with the current European guidelines for HF treatment dated 2012 [20] and the European guidelines for AF treatment dated 2012 [21].

Endpoints. The primary endpoint of the study was hospitalization due to HF worsening. Secondary endpoints were cardiovascular mortality, any thromboembolic complications (TEC) and major bleeding as defined by the International Society on Thrombosis and Hemostasis (ISTH) [22].

The study was conducted in accordance with the principles of Good Clinical Practice (GCP), which protect the rights of study participants, rules for ensuring their safety and compliance with the requirements on study validity. The study was approved by the Committee on Ethics in Clinical

Table 1

Demographic parameters, anamnesis data

Parameters	All patients (n=1003)	AF-HFpEF (n=387)	AF-HFmrEF (n=150)	AF-HFrEF (n=466)	Significance, p
Demographic parameters					
Age, years	68 (60;76)	72 (63;78)	67 (58;75)	66 (58;75)	<0,001
Age ⩾65 years, %	589 (58,7%)	270 (69,8%)	82 (54,7%)	237 (50,9%)	<0,001
Age ⩾75 years, %	310 (30,9%)	157 (40,6%)	38 (25,3%)	115 (24,7%)	<0,001
Female, %	437 (43,6%)	253 (65,4%)	64 (42,7%)	120 (25,8%)	<0,001
BMI ⩾30, %	360 (35,9%)	147 (38%)	62 (41,3%)	151 (32,4%)	0,076
Low physical activity, %	570 (56,8%)	191 (49,4%)	96 (64%)	283 (60,7%)	<0,001
Smoking					
Never smoked, %	603 (60,1%)	295 (76,2%)	84 (56%)	224 (48,1%)	<0,001
Gave up smoking, %	216 (21,5%)	53 (13,7%)	38 (25,3%)	125 (26,8%)	
Smoking, %	184 (18,3%)	39 (10,1%)	28 (18,7%)	117 (25,1%)	
Comorbidity					
Hypertension, %	653 (65,1%)	263 (68%)	108 (72%)	282 (60,5%)	0,012
Duration of hypertension, age	14 (10;20)	13 (10;20)	10 (7,5;20)	15 (10;20)	0,916
CHD, %	686 (68,4%)	271 (70%)	107 (71,3%)	308 (66,1%)	0,336
Diabetes mellitus, %	247 (24,6%)	89 (23%)	38 (25,3%)	120 (25,8%)	0,632
Anamnesis of stroke, TIA, %	158 (15,8%)	58 (15%)	22 (14,7%)	78 (16,7%)	0,747
Anamnesis of MI, %	382 (38,1%)	98 (25,3%)	61 (40,7%)	223 (47,9%)	<0,001
Peripheral vascular disease, %	502 (50%)	157 (40,6%)	74 (49,3%)	271 (58,2%)	<0,001
Impaired renal function, %	145 (14,5%)	45 (11,6%)	24 (16%)	76 (16,3%)	0,123
Liver function abnormality, %	101 (10,1%)	12 (3,1%)	20 (13,3%)	69 (14,8%)	<0,001
Family anamnesis					
Family history of early development of CHD	230 (22,9%)	78 (20,2%)	43 (28,7%)	109 (23,4%)	0,106
Hypertension in relatives	516 (51,4%)	231 (59,7%)	84 (56%)	201 (43,1%)	<0,001

Abbreviations: CHD — coronary heart disease, MI — myocardial infarction, BMI — body mass index, HFrEF — heart failure with reduced left ventricular ejection fraction, HFmrEF — heart failure with midrange left ventricular ejection fraction, HFpEF — heart failure with preserved left ventricular ejection fraction, TIA — transient ischemic attack, AF — atrial fibrillation.

Cardiology of the Federal State Budgetary Institution "National Medical Research Center of Cardiology" of the Ministry of Health of the Russian Federation and registered on clinicaltrials.gov (NCT02790801).

Statistical data analysis. Descriptive statistics were described in absolute frequencies or as a median and interquartile interval. Depending on variables type, the Mann-Whitney test, Pearson's chi-square, Fisher's exact test, and the nonparametric Kruskal-Wallis test by rank and median were used. The Kaplan-Meyer analysis was used to determine the time to the study's endpoints. A two-sided significance criterion of (p) <0,05 was considered statistically significant. Statistical data analysis was performed using STATISTICA 7.0 (StatSoft, USA) and RStudio version 1.0.136 with R packages version 3.3.1.

Results

General characteristics of patients. The register enrolled 1003 patients with HF in combination with AF. Almost half were with reduced left ventricular (LV) EF — 46,4% of patients, 38,6% and 15% of patients had preserved and midrange LV EF, respectively. The clinical characteristics of the patients are shown in Tables 1-3.

Patients with preserved LV EF were older (median age of 72 years (63;78) versus 67 years (58;75) in the HFmrEF group and 66 years (58;75) in the HFrEF group), p<0,001. The percentage of women was highest (65,4%) in the HFpEF group and lowest in the HFrEF group (25,8%), p<0,001. The majority of patients with HFpEF — 76,2%, never smoked, while in the groups of patients with HFmrEF and HFrEF, non-smoking patients, were less, 56% and 48,1%,

Table 2

Clinical characteristics of AF and HF severity

Parameters	All patients (n=1003)	AF-HFpEF (n=387)	AF-HFmrEF (n=150)	AF-HFrEF (n=466)	Significance, p
Duration of HF, months	40 (12;96)	48 (22,5;100)	36 (12;72)	48 (12;96)	0,265
Duration of AF, months	48 (15;96)	50 (24;108)	38 (12;89)	40 (12;96)	0,042
Age of HF onset, years	62,1 (54,7;70,1)	64 (57,5;72,9)	61,65 (54,15;70,3)	60,9 (52,9;67,8)	<0,0001
Age of AF onset, years	62 (54,25;70,7)	64,4 (57,9;72,6)	60,8 (50,88;70,22)	59,9 (51,5;68,55)	<0,0001
AF onset after HF	478 (47,7%)	197 (50,9%)	58 (38,7%)	223 (47,9%)	0,039
AF form					
Paroxysmal	276 (27,5%)	144 (37,2%)	30 (20%)	102 (21,9%)	<0,001
Persistent/ permanent	727 (72,5%)	243 (62,8%)	120 (80%)	364 (78,1%)	
BP					
Systolic BP, mmHg	130 (120;140)	140 (130;150)	130 (120;140)	120 (110;140)	<0,0001
Diastolic BP, mmHg	80 (70;90)	80 (80;90)	80 (70;90)	80 (70;80)	0,01
HR					
HR, beats/min	84 (70;100)	80 (68;90)	85,5 (75,25;90,75)	84 (75;97)	0,226
HR >100, n (%)	327 (32,6%)	103 (26,6%)	56 (37,3%)	168 (36,1%)	0,005
CHA_2DS_2-VASc, median, interquartile interval	4 (3;5)	5 (3;6)	4 (3;5)	4 (2;5)	<0,001
HAS-BLED, median, interquartile interval	3 (2;4)	5 (3;6)	4 (3;5)	4 (2;5)	<0,001
Severity of AF symptoms by EHRA	2 (2;3)	2 (2;2)	2 (2;2)	2 (2;3)	0,083

Abbreviations: BP — blood pressure, HF — heart failure, HFrEF — heart failure with reduced left ventricular ejection fraction, HFmrEF — heart failure with midrange left ventricular ejection fraction, HFpEF — heart failure with preserved left ventricular ejection fraction, AF — atrial fibrillation, HR — heart rate.

Table 3

Data of instrumental and laboratory methods of examination at the time of enrollment

Parameters	All patients (n=1003)	AF-HFpEF (n=387)	AF-HFmrEF (n=150)	AF-HFrEF (n=466)	Significance, p
LV EF, %	40 (35;58)	60 (55;65)	43 (40;46)	34 (29;37)	<0,0001
LV EDD, cm	5,6 (5;6,3)	5 (4,6;5,3)	5,9 (5,3;6,38)	6,2 (5,7;6,91)	<0,0001
LV ESD, cm	4,1 (3,2;5,05)	3,1 (3;3,6)	4,5 (4;5)	5 (4,5;5,7)	<0,0001
CTAR, %	57 (54;62)	56,5 (53;61)	60 (55;63)	57 (55;63)	0,086
Number of VPB/day,	122 (17;775,5)	40 (8;327,25)	79 (13;1163)	277 (78,5;1319)	0,029
BNP, pg/ml	300 (158,25;602,48)	245,5 (152,25;429,75)	317,5 (142,25;507,15)	490,5 (186,52;941,75)	0,008
NT-proBNP, pg/ml	536 (349,5;1085)	562 (425;968)	338 (327;353,5)	1484 (289;2866)	0,01
D-dimer, ug/ml	1,2 (0,35;4,75)	1,38 (0,22;109)	2 (0,24;187)	1,1 (0,49;1,65)	0,048

Abbreviations: VPB — ventricular premature beats, CTAR — cardio-thoracic area ratio, LV EDD — end-diastolic dimension, LV CSR — end-systolic dimension, LV — left ventricle, HFrEF — heart failure with reduced left ventricular ejection fraction, HFmrEF — heart failure with midrange left ventricular ejection fraction, HFpEF — heart failure with preserved left ventricular ejection fraction, EF — ejection fraction, AF — atrial fibrillation, BNP — brain natriuretic peptide, NT-proBNP — N-terminal propeptide of natriuretic hormone (B-type).

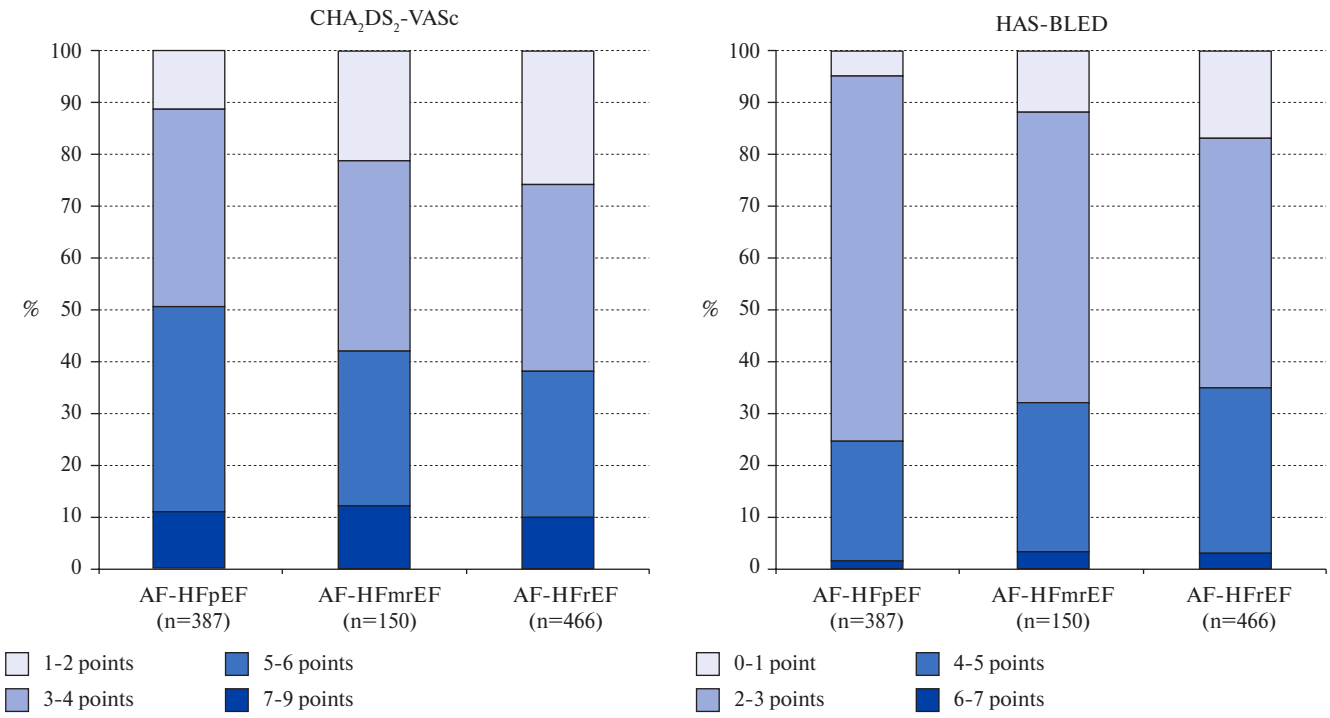

Figure 1. Assessment of TEC and bleeding risk.
Abbreviations: HFrEF — heart failure with reduced left ventricular ejection fraction, HFmrgEF — heart failure with midrange left ventricular ejection fraction, HFpEF — heart failure with preserved left ventricular ejection fraction, AF — atrial fibrillation.

respectively, p<0,001. Perhaps this is due to the fact that there were more women in the HFpEF group as a percentage. The groups of patients were comparable by frequency migrated with anamnesis of stroke or transient ischaemic attack, 15%, 14,7% and 16,7% in HFpEF groups, HFmrEF and HFrEF, respectively, p=0,747. In addition, the groups of patients were comparable by the frequency of occurrence of diabetes mellitus and impaired renal function. Significant differences in the groups were recorded by the frequency of myocardial infarction (MI), 25,3%, 40,7% and 47,9% in the HFpEF, HFmrEF and HFrEF groups, respectively, p<0,001. Also, patients with HFrEF most often suffered from peripheral arterial disease and liver function abnormality.

The patient groups did not differ significantly in the duration of heart failure before enrollment. Anamnesis of AF before enrollment to the register was higher in patients with HFpEF — median is 50 months (24;108), for patients with HFmrEF and HFrEF, the AF median duration before enrollment was 38 (12;89) and 40 (12;96) months, respectively, p=0,042. In groups of patients HFpEF and HFrEF (50,9% and 47,9%, respectively), the highest number of patients had a HF diagnosis before AF onset, and in the HFmrEF group, only in 38,7% of patients HF onset were before establishing the AF diagnosis, p=0,039.

The proportion of patients with paroxysmal AF was almost 2 times higher in the HFpEF group — 37,2% compared to patients from the HFmrEF and HFrEF groups (20% and 21,9%, respectively), p<0,001. In addition, patients with HFpEF had higher blood pressure numbers and a lower heart rate (HR). Only 26,6% of patients with HFpEF had heart rate >100 bpm, while in patients with HFmrEF and HFrEF, heart rate control was worse, heart rate >100 bpm was recorded in 37,3% and 36,1% of patients, respectively, p=0,005.

The study population had a high risk of TEC and bleeding, the median according to the CHA_2DS_2-VASc scale was 4 points (3;5), the median according to the HAS-BLED scale was 3 points (2;4). The groups of patients differed by the risk of TEC and bleeding, patients with HFpEF had higher scores according to both the CHA_2DS_2-VASc and HAS-BLED scales compared to patients with HFmrEF and HFrEF, p<0,001 (Figure 1, Table 2).

The drug therapy of patients in the registry is presented in Table 4. In the group of patients with HFpEF, the rate control strategy (p<0,001) was more often chosen and antiarrhythmic drugs were more often prescribed to these patients (p<0,001). It was noteworthy that only for 45,5% of patients with reduced LV EF the rational HF therapy were selected. For rational therapy in HF with reduced LV

Table 4

Drug therapy

Parameters	All patients (n=1003)	AF-HFpEF (n=387)	AF-HFmrEF (n=150)	AF-HFrEF (n=466)	Significance, p
Strategy of AF therapy					
Rhythm control	339 (33,8%)	157 (40,6%)	52 (34,7%)	130 (27,9%)	<0,001
HR monitoring	664 (66,2%)	230 (59,4%)	98 (65,3%)	336 (72,1%)	
Rational HF therapy	396 (39,5%)	106 (27,4%)	78 (52%)	212 (45,5%)	<0,001
Drugs group					
BB	830 (82,8%)	301 (77,8%)	136 (90,7%)	393 (84,3%)	<0,001
Antiarrhythmic drugs	255 (25,4%)	123 (31,8%)	37 (24,7%)	95 (20,4%)	<0,001
ACE inhibitors	658 (65,6%)	187 (48,3%)	113 (75,3%)	358 (76,8%)	<0,001
ARB	218 (21,7%)	116 (30%)	27 (18%)	75 (16,1%)	<0,001
MCRA	642 (64%)	164 (42,4%)	116 (77,3%)	362 (77,7%)	<0,001
Statins	606 (60,4%)	252 (65,1%)	89 (59,3%)	265 (56,9%)	0,046
Diuretics	883 (88%)	332 (85,8%)	131 (87,3%)	420 (90,1%)	0,137
Digoxin	360 (35,9%)	101 (26,1%)	53 (35,3%)	206 (44,2%)	<0,001
Oral anticoagulants (Warfarin/NOAC)	738 (73,6%)	297 (76,7%)	121 (80,7%)	320 (68,7%)	<0,001
Warfarin	403 (40,2%)	157 (40,6%)	66 (44%)	180 (38,6%)	0,491
NOAC	335 (33,4%)	140 (36,2%)	55 (36,7%)	140 (30%)	0,107
Antiplatelet agents	466 (46,5%)	177 (45,7%)	61 (40,7%)	228 (48,9%)	0,200

Abbreviations: MCRA — mineralocorticoid receptor antagonists, BB — beta-blockers, ARB — angiotensin II receptor blockers, ACE inhibitors — angiotensin-converting enzyme inhibitors, NOAC — novel oral anticoagulant, HF — heart failure, HFrEF — heart failure with reduced left ventricular ejection fraction, HFmrgEF — heart failure with midrange left ventricular ejection fraction, HFpEF — heart failure with preserved left ventricular ejection fraction, AF — atrial fibrillation, HR — heart rate.

Table 5

Outcomes of patients with HF in combination with AF

Endpoints	All patients (n=1003)	AF-HFpEF (n=387)	AF-HFmrEF (n=150)	AF-HFrEF (n=466)	Significance, p
Hospitalization due to HF worsening	574 (57,2%)	204 (52,7%)	99 (66%)	271 (58,2%)	0,017
Cardiovascular mortality	102 (10,2%)	16 (4,1%)	14 (9,3%)	72 (15,5%)	<0,001
Thromboembolic events	34 (3,4%)	14 (3,6%)	7 (4,7%)	13 (2,8%)	0,451
Ischemic stroke	27 (2,7%)	12 (3,1%)	4 (2,7%)	11 (2,4%)	0,776
Myocardial infarction	101 (10,1%)	26 (6,7%)	20 (13,3%)	55 (11,8%)	0,014
Composite point (stroke, MI, cardiovascular mortality)	201 (17%)	49 (12,7%)	33 (22%)	119 (25,5%)	<0,001
Major bleeding	39 (3,9%)	15 (3,9%)	7 (4,7%)	17 (3,6%)	0,815

Abbreviations: MI — myocardial infarction, HF — heart failure, HFrEF — heart failure with reduced left ventricular ejection fraction, HFmrgEF — heart failure with midrange left ventricular ejection fraction, HFpEF — heart failure with preserved left ventricular ejection fraction, AF — atrial fibrillation.

EF, we assumed the presence of angiotensin-converting enzyme inhibitors (ACE inhibitors)/angiotensin II receptor blockers (ARBs), beta-blockers (BBs), mineralocorticoid receptor antagonists (MCRA) in the treatment regimen in doses exceeding 50% of target values, as well as diuretics in the presence of fluid retention symptoms. The frequency of ordering long-term anticoagulant treatment in the study population was 73,6%, 40,2% of patients took Warfarin and 33,4% were under therapy with novel oral anticoagulants (NOAC). The most common anticoagulant treatment was prescribed to patients with HFmrEF — 80,7% of patients, with HFpEF and HFrEF, the frequency of prescribing anticoagulant treatment was lower — 76,7% and 68,7%, respectively, p<0,001.

Results of follow-up of patients in the course of 12 months. In the course of 12 months of follow-up, 57,2% of patients were hospitalized at least once due to HF decompensation. The highest frequency

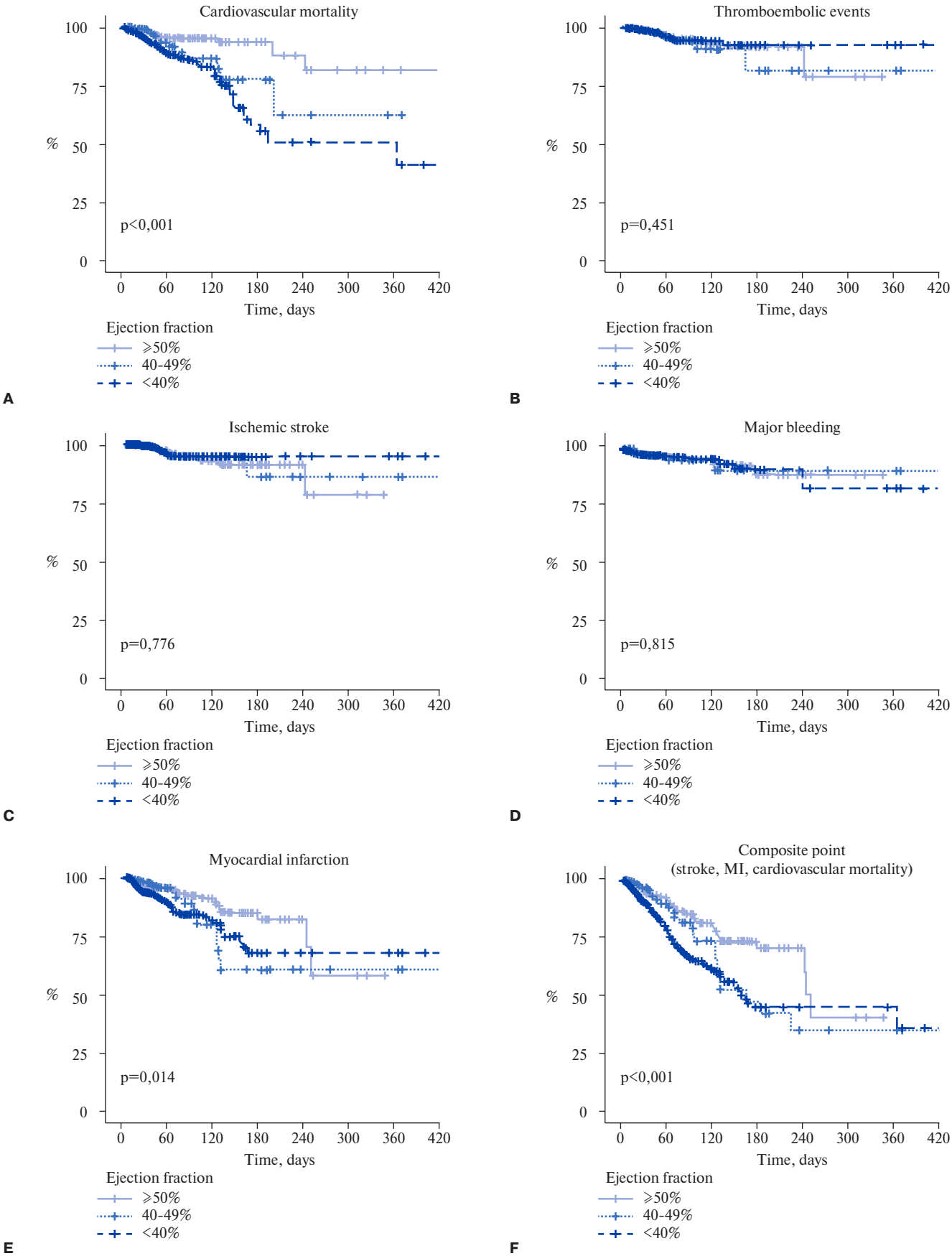

Figure 2. Kaplan-Mayer curves for subgroups by LV EF.

Table 6

Univariate regression logistic analysis of the hospitalization risk due to HF decompensation

Group of factors	Factor	AF-HFpEF		AF-HFmrEF		AF-HFrEF	
		RR (2,5-97,5)	p	RR (2,5-97,5)	p	RR (2,5-97,5)	p
Demographic profile	Age >65 years	2,329 (1,462-3,745)	<0,001			1,736 (1,17-2,584)	0,006
	Female	1,866 (1,198-2,921)	0,006				
Lifestyle, habits	Smoking (ever)	1,852 (1,073-3,236)	0,028				
	Bad habits	2,009 (1,107-3,723)	0,023				
	Alcohol abuse					1,37 (1,038-1,828)	0,028
	Physical activity			0,549 (0,274-1,081)	0,085	0,616 (0,399-0,944)	0,027
Symptoms and syndromes	HF signs	1,482 (1,146-1,946)	0,003				
	Increased venous pressure					2,383 (1,02-5,847)	0,048
	HF symptoms					2,275 (1,1-4,844)	0,028
Concurrent diseases	Diabetes mellitus	1,733 (1,048-2,908)	0,034				
Cardio-vascular system	Arterial hypertension					2,347 (1,524-3,663)	<0,001
	Tricuspid insufficiency	1,408 (1,027-1,949)	0,036				
	Aortic valve insufficiency	1,721 (1,074-2,865)	0,028				
	Insufficiency on pulmonary artery valve	3,69 (1,46-10,87)	0,01				
	Significant coronary artery stenosis					2,166 (1,276-3,8)	0,005
	CTAR, %					1,138 (1,047-1,244)	0,003
	Peripheral vascular diseases	1,73 (1,126-2,673)	0,013				
	Anamnesis of stroke/TIA/ thromboembolism	1,866 (1,198-2,921)	0,006				
Treatment	Antiarrhythmic drugs	0,622 (0,393-0,978)	0,041				
	ACE inhibitors	0,582 (0,371-0,907)	0,017				
	CCB at constant AF	0,505 (0,311-0,812)	0,005				
	ARB	0,466 (0,288-0,745)	0,002			0,587 (0,331-1,01)	0,06
	Anticoagulants					0,389 (0,257-0,587)	<0,001
	BB at continuous AF					0,279 (0,152-0,496)	<0,001
	Rational HF therapy					0,409 (0,271-0,611)	<0,001
	MCRA					0,584 (0,361-0,942)	0,027
	NOAC					0,588 (0,377-0,907)	0,017
	Heart rate control strategy (vs rhythm control)	1,779 (1,156-2,747)	0,009			0,283 (0,125-0,599)	<0,001
AF/HF features	Development of HF after AF onset	2,002 (1,049-3,879)	0,037				
	Duration of AF	1,005 (1,001-1,01)	0,022				
	Duration of HF					1,005 (1,002-1,009)	0,003
	EF					0,958 (0,922-0,995)	0,026
	Persistent form of AF (vs paroxysmal)	0,464 (0,296-0,722)	0,001			2,755 (1,451-5,405)	0,002
Risk of TEC/ bleeding	CHA_2DS_2-VASc	1,393 (1,215-1,608)	<0,001	1,191 (0,981-1,46)	0,083	1,215 (1,089-1,359)	0,001
	HAS-BLED	1,461 (1,174-1,836)	0,001			1,196 (1,014-1,414)	0,035

Abbreviations: MCRA — mineralocorticoid receptor antagonists, BB — beta-blockers, CCB — calcium channel blockers, ARB — angiotensin II receptor blocker, ACE inhibitors — angiotensin-converting enzyme inhibitors, CTAR — cardio-thoracic area ratio, NOAC — novel oral anticoagulant, RR — risk ratio, HF — heart failure, HFrEF — heart failure with reduced fraction left ventricular ejection, HFmrgEF — heart failure with midrange left ventricular ejection fraction, HFpEF — heart failure with preserved left ventricular ejection fraction, TIA — transient ischaemic attack, TEC — thromboembolic complications, AF — atrial fibrillation, Heart Rate — heart rate.

Table 7

Univariate logistic regression analysis of cardiovascular mortality risk

Group of factors	Factor	AF-HFpEF		AF-HFmrEF		AF-HFrEF	
		RR (2,5-97,5)	p	RR (2,5-97,5)	p	RR (2,5-97,5)	p
Laboratory tests	Total cholesterol			0,515 (0,291-0,851)	0,014		
	INR	2,825 (1,353-7,937)	0,013				
Symptoms and syndromes	Anemia	5,618 (1,799-16,667)	0,002	4,219 (1,156-14,286)	0,022		
	HF signs	2,299 (1,441-3,676)	<0,001	1,567 (0,924-2,653)	0,089	1,497 (1,163-1,927)	0,002
	HF symptoms	1,961 (1,335-2,941)	0,001			1,346 (1,121-1,629)	0,002
Concurrent diseases	Erosive and ulcerative lesions of gastrointestinal tract according to endoscopy					2,353 (0,951-5,464)	0,053
	Liver function abnormality			5,291 (1,425-18,519)	0,009		
	Renal disorder	4,184 (1,245-12,5)	0,013				
Cardio-vascular system	Aortic valve insufficiency			2,907 (0,915-10,101)	0,075		
	Arterial hypertension					2 (1,089-3,891)	0,032
	CTAR, %	1,597 (1,133-2,841)	0,036			1,161 (1,053-1,294)	0,004
	Anamnesis of MI and/or stroke	3,521 (1,222-11,494)	0,024				
	Insufficiency on pulmonary artery valve					2,725 (1,269-5,882)	0,009
	Right atrium enlargement					3,546 (1,235-14,925)	0,04
	Tricuspid insufficiency					1,37 (0,983-1,908)	0,061
	Echocardiographic signs of previous MI	3,636 (1,233-10,526)	0,016			1,957 (1,129-3,509)	0,02
	Dilation of pulmonary artery					2,375 (1,224-4,608)	0,01
	Anamnesis of major bleeding	6,494 (2,174-19,231)	0,001	3,891 (1,073-13,158)	0,03		
Treatment	Anticoagulants					0,389 (0,225-0,666)	0,001
	NOAC					0,42 (0,202-0,806)	0,013
	Peripheral vasodilators					4,587 (1,695-11,905)	0,002
	Statins	0,254 (0,083-0,724)	0,011			0,627 (0,366-1,08)	0,089
	ACE inhibitors	0,22 (0,069-0,84)	0,015				
	BB at continuous AF					0,404 (0,213-0,791)	0,006
	CCB at constant AF	0,172 (0,009-0,872)	0,091				
	Rational HF therapy					0,432 (0,238-0,757)	0,004
AF/HF features	Development of HF after AF onset					0,463 (0,209-0,987)	0,05
	Age of AF onset					1,037 (1,011-1,067)	0,007
	HR >100 bpm			4,545 (0,917-33,333)	0,081		
Risk of TEC/ bleeding	CHA_2DS_2-VASc	1,385 (1,029-1,869)	0,031			1,163 (1,01-1,342)	0,037
	HAS-BLED	2,105 (1,305-3,425)	0,002	1,938 (1,238-3,175)	0,005	1,37 (1,098-1,715)	0,006

Abbreviations: BB — beta-blockers, CCB — calcium channel blocker, ACE inhibitors — angiotensin-converting enzyme inhibitors, GIT — gastrointestinal tract, MI — myocardial infarction, CTAR — cardio-thoracic area ratio, INR — international normalized ratio, NOAC — novel oral anticoagulants, RR — risk ratio, HF — heart failure, HFrEF — heart failure with reduced left ventricular ejection fraction, HFmrgEF — heart failure with mid-range left ventricular ejection fraction, HFpEF — heart failure with preserved left ventricular ejection fraction, TEC — thromboembolic complications, AF — atrial fibrillation, HR — heart rate.

Table 8

Univariate regression logistic analysis of MI risk

Group of factors	Factor	AF-HFpEF		AF-HFmrEF		AF-HFrEF	
		RR (2,5-97,5)	p	RR (2,5-97,5)	p	RR (2,5-97,5)	p
Laboratory tests	Triglycerides					1,566 (1,11-2,362)	0,02
Demographics specifications	Age >65 years	3,115 (1,044-13,398)	0,071	3,27 (1,099-12,063)	0,047		
Lifestyle, habits	Physical activity	0,455 (0,173-1,069)	0,086				
	Poor nutrition					4,714 (1,363-29,721)	0,038
Symptoms and syndromes	Signs of AH (loud second heart sound on PA, LVH)	3,242 (1,269-9,964)	0,022	10,108 (1,969-185,253)	0,027		
	Anemia					1,964 (0,84-4,21)	0,097
	HF signs	1,87 (1,256-2,754)	0,002	1,962 (1,237-3,208)	0,005		
Concurrent diseases	Liver function abnormality			4,417 (1,34-13,764)	0,011		
Cardio-vascular system	Aortic valve insufficiency	0,418 (0,148-1,045)	0,082	7,368 (2,457-27,37)	0,001	3,427 (1,565-7,683)	0,002
	Peripheral vascular diseases	8,226 (3,029-28,777)	<0,001				
	Pathological changes on electrocardiogram			10,88 (2,92-70,815)	0,002		
	Anamnesis of MI and/or stroke	9,643 (3,547-33,762)	<0,001				
	Cardiomyopathy	1,591 (0,827-2,635)	0,096	1,68 (0,88-2,999)	0,086	1,528 (0,947-2,371)	0,068
	Family history of early development of CHD			0,256 (0,039-0,972)	0,08	1,911 (1,009-3,569)	0,044
	Significant coronary artery stenosis			3,316 (1,1-9,569)	0,028	2,036 (1,025-3,888)	0,035
	Anamnesis of coronary artery stenting	3,311 (1,131-8,591)	0,019	4,727 (1,528-14,174)	0,006	2,043 (0,99-4,011)	0,044
	Anamnesis of PATE	5,873 (0,809-29,014)	0,041	5,7 (1,041-28,378)	0,032		
	Tricuspid insufficiency					1,601 (1,105-2,323)	0,013
	Venous thrombosis of lower limbs	4,543 (0,966-16,216)	0,03	9 (0,76-127,873)	0,078		
	Echocardiographic signs of previous MI	9,509 (3,986-24,457)	<0,001	10,51 (2,822-68,395)	0,002	4,459 (2,144-10,482)	<0,001
	Dilation of pulmonary artery	4,165 (1,47-11,651)	0,006	9,797 (2,931-39,334)	<0,001	2,727 (1,323-5,652)	0,006
Treatment	Rivaroxaban			0,114 (0,006-0,79)	0,057		
	Digoxin			0,324 (0,072-1,051)	0,088		
	ACE inhibitors			0,407 (0,147-1,158)	0,084		
	Ivabradine					6,313 (1,516-24,687)	0,007
AF/HF features	Development of HF after AF onset	3,154 (1,026-11,799)	0,058			0,471 (0,19-1,101)	0,089
	Age of HF onset	1,051 (1,005-1,101)	0,033	1,045 (0,996-1,102)	0,082		
	Persistent AF form					0,158 (0,009-0,752)	0,071
	Resting HR			0,382 (0,143-0,945)	0,043		
Risk of TEC/ bleeding	CHA_2DS_2-VASc	1,372 (1,077-1,752)	0,01	1,398 (1,069-1,865)	0,017		
	HAS-BLED			1,609 (1,09-2,432)	0,019		

Abbreviations: AH — arterial hypertension, LVH — left ventricular hypertrophy, ACE angiotensin-converting enzyme inhibitors, CHD — coronary heart disease, MI — myocardial infarction, PA — pulmonary artery, RR — risk ratio, HF — heart failure, HFrEF — heart failure with reduced left ventricular ejection fraction, HFmrgEF — heart failure with midrange left ventricular ejection fraction, HFpEF — heart failure with preserved left ventricular ejection fraction, PATE — pulmonary artery thromboembolia, TEC — thromboembolic complications, AF — atrial fibrillation, HR — heart rate.

of hospitalizations was observed in the group with HFmrEF (66%), patients with HFpEF were less often hospitalized (52,7%), p=0,017 (Table 5). In the study, significant differences in cardiovascular death incidence depending on LV EF were noted. Increased mortality rate was associated with reduced LV EF, as a result, cardiovascular mortality in patients with HFpEF was 4,1%, in the HFmrEF and HFrEF groups — 9,3% and 15,5%, respectively, p<0,001 (Table 5, Figure 2 A).

The TEC frequency in the total patient cohort in the course of 12 months was 3,4%, ischemic stroke was suffered by 2,7% of patients, these indicators did not depend on LV EF (Figure 2 B, C). It is worthy of note that several patients (10 patients — 1% of the sample) had 2 different events during the year (for example, ischemic stroke and pulmonary artery thromboembolia (PATE). The study reported 39 major bleeding (3,9%), of whom 13 (1,3%) cases of gastrointestinal bleeding, 6 (0,6%) — pulmonary hemorrhage, 5 (0,5%) — intracranial bleeding and 15 (1,5%) bleeding at other sites (Figure 2 D).

In the course of 12 months of follow-up, 101 (10,1%) new cases of MI were registered in the total patient cohort. In the vast majority of cases, MIs (96 out of 101) were recurrent. Among the enrolled patients who had anamnesis of MI, the frequency of recurrent MI was 25.1%, while the incidence rate of the first MI was low — 0,8%, p<0,001. There were statistically significant differences in the frequency of MI between patients depending on LV EF, the lowest frequency was observed in patients with HFpEF — 6,7%, p=0,014 (Figure 2 E). In addition, in the group of patients with HFpEF, the lowest frequency of reaching the combined endpoint (stroke, MI, cardiovascular mortality), 12,7%, was demonstrated, in the HFmrEF and HFrEF groups the frequency of achieving the composite endpoint was 22% and 25,5%, respectively, p<0,001 (Figure 2 E).

Predictors of unfavorable prognosis. We carried out a search and analysis of factors influencing the achievement of endpoints in the study for the three groups of patients: HFpEF, HFmrEF and HFrEF. The analysis of factors related to outcomes led us to the conclusion that RF of adverse outcomes significantly differ for the groups depending on EF. However, it is important to note that the groups had significant differences in a number of parameters that were described above. Predictors of hospitalization due to HF decompensation in the group of patients with HFpEF were age >65 years, female sex, smoking, diabetes mellitus, peripheral artery atherosclerosis, stroke or transient ischaemic attack in the anamnesis, HF onset after AF development. The predictors of hospitalization for patients with HFrEF due to HF decompensation were age >65 years, arterial hypertension, and hemodynamically significant coronary artery stenosis. Symptoms were more predictive in terms of hospitalization for patients with HFrEF and HF signs — for patients with HFpEF. Persistent AF compared to paroxysmal reduced the hospitalization risk with HFpEF and increased the frequency of hospitalizations in patients with HFrEF. The choice of HR control strategy compared to rhythm control increased the hospitalization risk in patients with HFpEF and reduced it in patients with HFrEF. In patients with HFpEF, the hospitalization risk was reduced with regular administration of antiarrhythmic drugs, calcium antagonists, persistent AF, renin-angiotensin-aldosterone system (RAAS) blockers. For patients with HFrEF, the hospitalization risk was reduced by taking anticoagulants, in particular, taking NOACs, as well as BBs, MCRAs, RAAS blockers and rational therapy of HF, which included BBs, RAAS antagonists, and MCRAs. In addition, patients with high scores according to the CHA_2DS_2-VASc and HAS-BLED scales had a higher hospitalization risk (Table 6).

RF of cardiovascular mortality also had differences by group depending on LV EF. Predictors of cardiovascular mortality in patients with intermediate LV EF were anemia, liver function abnormality, anamnesis of major bleeding, and a high risk of bleeding according to the HAS-BLED scale. HF symptoms and signs, signs of MI according to echocardiography, as well as a high risk of TEC and bleeding according to the CHA_2DS_2-VASc and HAS-BLED scales were common RF of cardiovascular mortality for patients with HFpEF and HFrEF. Significant RF for patients with HFpEF were impaired renal function and anamnesis of major bleeding, and the risk of death was reduced by taking statins and ACE inhibitors. For patients with HFrEF, arterial hypertension, pulmonary artery regurgitation, dilation of pulmonary trunk, right atrium enlargement were predictors of cardiovascular mortality, and the risk of death was reduced by taking anticoagulants, BBs and rational therapy of CHF, in addition, the risk of death was lower if HF developed later than the AF onset (Table 7).

The MI RFs assessment showed that for patients with HFpEF, HFmrEF and HFrEF, the common RFs were anamnesis of stent angioplasty of coronary arteries and zones of impaired local contractility according to echocardiography. In addition, the predictors of MI in patients with HFpEF were HF signs during objective examination, anamnesis of peripheral artery disease, anamnesis of stroke/MI, anamnesis of PATE and a high risk of TEC according to the CHA_2DS_2-VASc scale. MI RF were in patients with HFREF over 65 years of age, signs of HF on physical examination, liver function

abnormality, known stenosis of coronary arteries, a anamnesis of PATE, as well as a high calculated risk of TEC and bleeding. Increased triglyceride levels, known coronary artery stenosis, and a burdened family anamnesis of coronary heart disease were predictors of MI in HFrEF patients (Table 8).

Discussion

The goal of our study was to analyze the features of CHF diagnosis and treatment in patients with AF to assess patient outcomes and degree of compliance with clinical recommendations for CHF and AF treatment in the Russian Federation. The primary study's endpoint was hospitalization due to HF worsening. According to the follow-up results in the course of 12 months, the frequency of hospitalizations due to HF decompensation was 57,2%. The greatest risk of hospitalization were patients with HFmrEF. Cardiovascular mortality, any feasibility studies, and major bleeding were taken as secondary endpoints. It was identified that the risk of cardiovascular death in the study increased in parallel with the LV EF decrease. Despite the fact that patients with HFpEF had a higher estimated TEC risk, the incidence rate of ischemic stroke is not dependent on LV EF. Patients with HFpEF had the lowest risk of reaching the composite endpoint (stroke, MI, cardiovascular mortality) in comparison with patients with HFmrEF and HFrEF.

According to the EPOCHA-CHF's study [23], 56,8% of patients with CHF in Russia have preserved LV EF, in our study, the number of patients with preserved LV EF was lower — 38,6%. This can be ascribed to the fact that the majority of patients were enrolled in inpatient facility, which indicates the disease severity in the studied subgroup. Also worth noting is that our study enrolled patients with proven elevated levels of natriuretic peptides, whereas the EPOCHA-CHF's study used different criteria for establishing the HFpEF diagnosis.

According to our data, CHF rational treatment, as well as long-term anticoagulant treatment, are determining factors in reducing the risk of hospitalization and cardiovascular mortality in patients with HFrEF. In spite of that, the therapy in the studied cohort was suboptimal. In the group of patients with HFrEF, ACE inhibitors was taken by 76,8% of patients, ARBs — 16,1% of patients, BBs — 84,3%, MCRAs — 77,7%. The insufficient level of compliance with clinical recommendations can be found in many observational studies in comparison with data from randomized clinical studies. Thus, in the EORP-AF registry, ACE inhibitors was taken by 48% of patients, ARBs — 21%, BBs — 72,2%, diuretics — 59,2% [24]. In the QUALIFY register (n=7092), the level of compliance with clinical recommendations for the CHF treatment was assessed, the authors analyzed the frequency of prescribing ACE inhibitors, ARBs, BBs, MCRAs and ivabradine. The level of compliance with recommendations was good in 67%, moderate — in 25% and poor — in 8% of patients. The proportion of patients who received the target dose of drugs or ⩾50% of the target dose was low (27,9% and 63,3% for ACE inhibitors, 14,8% and 51,8% for BBs, 6,9% and 39,5% for ARBs, 70,8% and 99,1% for AMCRs, 26,6% and 86,4% for ivabradine, respectively) [25]. The therapy that the patients in our study received had a great impact on the hospitalization frequency. For patients with HFrEF, the most important factor was whether they received anticoagulant treatment and its type. Rational therapy (RAAS antagonist+BB+AMCR) significantly reduced the risk of re-hospitalization. In a prospective multicenter AF-CHF study, the BB use was associated with a reduction in mortality rate, but did not reduce the hospitalization frequency in patients with HFrEF and AF without regard for the AF form or burden [26]. These data differ from the results of the meta-analysis by Kotecha D, et al. [16], according to which BBs in patients with HFrEF and AF did not reduce the mortality rate from all causes, the risk ratio was 0,97 compared to placebo (95% confidence interval (CI) 0,83-1,14) as against patients with sinus rhythm — 0,73 (95% CI 0,67-0,880), p=0,002. In the work of Rienstra M, et al., it was concluded that the effect of beta-blockers in patients with CHF and AF is significantly different from the effect of these drugs in patients with CHF and sinus rhythm, however, they do not have a positive effect on the hospitalization frequency due to CHF decompensation or mortality rate [27].

All patients with AF and HF have strict indications for appointment of anticoagulant treatment. Taking anticoagulants is a proven method to influence the prognosis of patients with CHF in combination with AF [17], but the results of multicenter registries by the AF problem, such as GARFIELD (The Global Anticoagulant Registry in the FIELD) [28] and Euro Heart Survey AF [29], show a significant gap between clinical recommendations for patient management and actual clinical practice. The frequency of prescribing long-term anticoagulant treatment in the population of patients in our study was 73,6%. In the Euro Heart Survey AF registry, 32% of patients did not receive anticoagulant treatment in the absence of contraindications [29]. The GARFIELD's results show that 38% of patients with risk of TEC according to the $CHADS_2$ scale ⩾2 did not receive anticoagulants, while 42,5% of low-risk patients ($CHADS_2$ =0) received anticoagulant treatment [28]. According

to a meta-analysis by Kotecha D, et al. (n=54,587) the frequency of prescribing anticoagulant treatment in patients with CHF in combination with AF is even lower (especially in cohort studies), 49,9% and 54,8% for patients with HFpEF and HFrEF, respectively [30]. A meta-analysis by Savarese G, et al. (n=55011) shows that although patients with HF in combination with AF have a higher mortality rate, if they take anticoagulants, the frequency of TEC and major bleeding in them does not differ from patients without HF [31]. The above once again emphasizes the need for appointment of anticoagulant treatment in patients with CHF in combination with AF.

Congestive HF is an independent RF of stroke in AF [32]. In large observational studies, it was observed that the prevalence of AF was higher in patients with HFpEF. This is thought to be related to the increased left atrial stiffness observed in HFpEF, while HFrEF is connected with eccentric left atrial remodeling [33]. According to the results of ESC-HF Long-Term Registry, the incidence of AF in patients with HFrEF, HFmrEF and HFpEF was 27%, 29% and 39%, respectively [34]. In the Swedish HF registry, patients were older and the incidence of AF was higher — 53%, 60%, and 65% in patients with HFrEF, HFmrEF, and HFpEF, respectively, but, as in the previous study, patients with HFpEF were dominant [35]. According to the analysis of a subgroup of patients with CHF in the PREFER register in AF, patients with HFpEF had a higher risk of TEC according to the CHA_2DS_2-VASc scale compared to patients with HFrEF and HFmrEF (4,7 vs 4,1 and 4,4, respectively). Despite this, the number of strokes in the group of patients with HFpEF was lower compared to the other two groups (0,65% vs 1,71% in HFmrEF; 1,75% in HFrEF; p=0,014). It was found that the risk of stroke increased by 0,054% with a 1% decrease in LV EF (95% CI 0,013-0,096; p=0,031), and in patients taking anticoagulants (90% of cohort), the risk of stroke increased by 0,030% with a 1% decrease in LV EF (95% CI 0,011-0,048; p=0,003). The TEC predictors in patients with AF in combination with HF were reduced LV EF, NYHA class, and age [36]. This is an interesting observation, because despite the lower estimated risk of stroke according to the CHA_2DS_2-VASc scale, a decrease in LV EF was associated with an increase in the frequency of strokes. In addition, it is worth noting that the CHA_2DS_2-VASc scale does not take into account EF in CHF. In our study, patients with HFpEF also had a higher risk of TEC according to the CHA_2DS_2-VASc scale, but we did not find significant differences in the TEC frequency depending on LV EF.

We did not find significant differences between the groups by frequency of major bleeding, the small number of events did not allow us to analyze the RF of bleeding.

The strategy selection for controlling the rhythm or HR in patients with CHF in combination with AF has significant differences depending on LV EF. The effectiveness of two AF therapeutic strategies in patients with HFrEF was compared in the AF-CHF study [26]. There were no significant differences in level of total or cardiovascular mortality, the frequency of stroke and hospitalizations due to HF decompensation between the two groups. Perhaps, the lack of effectiveness of pharmacological rhythm control is explained by shortcomings of modern antiarrhythmic drugs, which do not always provide stable retention of the sinus rhythm and cause adverse effects, in particular, have proarrhythmic effects. Drug-free treatments, such as catheter ablation, can serve as an alternative to antiarrhythmic therapy. Currently, there are data from the CASTLE-AF study, which showed the effect of catheter ablation on rigid endpoints in patients with HFrEF and AF [37]. The evidence base regarding the selection of control strategy of rhythm or HR in patients with AF and HFpEF is limited. Analysis of the GWTG-HF register (n=15682) shows that the selection of control strategy of rhythm has advantages over HR control in patients with HFpEF and AF over 65 years of age. The selection of rhythm control tactics was associated with a decrease in overall mortality during the year of follow-up, risk ratio 0,86; 95% CI 0,75-0,98; p=0,02 [38]. In our study, the selection of control strategy of rhythm and the use of antiarrhythmic drugs reduced the hospitalization frequency in HFpEF patients.

According to the data received, patients with HFrEF had the highest rates of cardiovascular death, in addition, HFrEF was associated with the achievement of composite endpoint (stroke, MI, cardiovascular mortality). The similar data were received in a meta-analysis by Kotecha D, et al. (n=54587), patients with HFrEF and AF had a higher mortality rate compared to patients with HFpEF and AF, 24% vs 18%, respectively, p=0,02 [30]. It is worth noting that, as in our study, the frequency of strokes between the groups did not differ depending on LV EF in this meta-analysis. However, whether AF independently connected with worse prognosis, with HFrEF remains controversial and poorly understood in HFpEF and HFmrEF. According to ESC-HFA HF Long-Term Registry (n=14964), the presence of AF was associated with an increased hospitalization risk due to decompensation of CHF and composite endpoint (hospitalization due to CHF decompensation + overall mortality) in patients with HFpEF and HFmrEF, but not HFrEF in comparison with similar groups of patients with sinus rhythm [34].

Oppositely, the results of Swedish Heart Failure Registry (n=41446) show that AF is connected with an increased risk of death, hospitalization due to decompensation of CHF and stroke in all groups by EF [35].

The group of patients with HFmrEF significantly differed from the other two groups in relation to the achievement of primary endpoint. In this group, the percentage of re-hospitalized patients was significantly higher. We found that each group was characterized by its own factors related to the primary endpoint.

Our study has a number of limitations. Despite the large pool of patients enrolled in it, the compared groups had significant initial differences. Due to the insufficient use of surgical methods for the CHF treatment, data on implantation of a cardioverter-defibrillator, cardiac resynchronization therapy, and catheter ablation were not included in the statistical analysis. Nevertheless, we have accumulated a large amount of data that reflects the real situation in clinical practice for our country and can be associate with works from other countries. Our goal was to study the differences between the groups depending on LV EF and to determine the predictors of adverse outcomes. We investigated how modern clinical practice in Russia meets international recommendations. This study was the first in our country and enrolled patients from 23 regions of Russia.

Conclusion

Each subgroup of patients, depending on LV EF, has specific features of the CHF and AF course, and the risks and predictors of adverse outcomes for these subgroups are different. Low LV EF is associated with an increased risk of death from cardiovascular diseases, but not with the risk of TEO (such as stroke and systemic embolism). Rational treatment of CHF and long-term anticoagulant treatment are key factors that reduce the risk of re-hospitalization and cardiovascular mortality in patients with HFrEF. The heart rate control strategy has some advantages associated with a reduced hospitalization risk due to CHF decompensation in patients with HFrEF, while the rhythm control strategy is more useful for patients with HFpEF.

Relationships and Activities: none.

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