

# Combination of Atrial Fibrillation and Coronary Heart Disease in Patients in Clinical Practice: Comorbidities, Pharmacotherapy and Outcomes (Data from the RECVASA Registries)

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**Aim.** Assess the structure of comorbid conditions, cardiovascular pharmacotherapy and outcomes in patients with atrial fibrillation (AF) and concomitant coronary artery disease (CAD) included in the outpatient and hospital RECVASA registries.

**Materials and methods.** 3169 patients with AF were enrolled in outpatient RECVASA (Ryazan), RECVASA AF-Yaroslavl registries and hospital RECVASA AF (Moscow, Kursk, Tula). 2497 (78.8%) registries of patients with AF had CAD and 703 (28.2%) of them had a previous myocardial infarction (MI).

**Results.** There were 2,497 patients with a combination of AF and CAD (age was  $72.2 \pm 9.9$  years; 43.1% of men; CHA<sub>2</sub>DS<sub>2</sub>-VASc –  $4.57 \pm 1.61$  points; HAS-BLED –  $1.60 \pm 0.75$  points), and the group with AF without CAD included 672 patients (age was  $66.0 \pm 12.3$  years; 43.2% of men; CHA<sub>2</sub>DS<sub>2</sub>-VASc –  $3.26 \pm 1.67$  points; HAS-BLED –  $1.11 \pm 0.74$  points). Patients with CAD were on average 6.2 years older and had a higher risk of thromboembolic and hemorrhagic complications ( $p < 0.05$ ). 703 patients with a combination of AF and CAD had the previous myocardial infarction (MI; age was  $72.3 \pm 9.5$  years; 55.2% of men; CHA<sub>2</sub>DS<sub>2</sub>-VASc –  $4.57 \pm 1.61$ ; HAS-BLED –  $1.65 \pm 0.76$ ), and 1794 patients didn't have previous MI (age was  $72.2 \pm 10.0$  years; 38.4% of men; CHA<sub>2</sub>DS<sub>2</sub>-VASc –  $4.30 \pm 1.50$ ; HAS-BLED –  $1.58 \pm 0.78$ ). The proportion of men was 1.4 times higher among those with the previous MI. Patients with a combination of AF and CAD significantly more often ( $p < 0.0001$ ) than in the absence of CAD received a diagnosis of hypertension (93.8% and 78.6%), chronic heart failure (90.1% and 51.2%), diabetes mellitus (21.4% and 13.8%), chronic kidney disease (24.8% and 17.7%), as well as anemia (7.0% and 3.0%;  $p = 0.001$ ). Patients with and without the previous MI had the only significant difference in the form of a diabetes mellitus higher incidence having the previous MI (27% versus 19.2%,  $p = 0.0008$ ). The frequency of proper cardiovascular pharmacotherapy was insufficient, mainly in the presence of CAD (67.8%) than in its absence (74.5%), especially the prescription of anticoagulants (39.1% and 66.2%;  $p < 0.0001$ ), as well as in the presence of the previous MI (63.3%) than in its absence (74.3%). The presence of CAD and, in particular, the previous MI, was significantly associated with a higher risk of death (risk ratio [RR] = 1.58; 95% confidence interval [CI] was 1.33-1.88;  $p < 0.001$  and RR = 1.59; 95% CI was 1.33-1.90;  $p < 0.001$ ), as well as with a higher risk of developing a combined cardiovascular endpoint (RR = 1.88; 95% CI was 1.17-3.00;  $p < 0.001$  and RR = 1.75; 95% CI was 1.44-2.12;  $p < 0.001$ , respectively).

**Conclusion.** 78.8% of patients from AF registries in 5 regions of Russia were diagnosed with CAD, of which 28.2% had previously suffered myocardial infarction. Patients with a combination of AF and CAD more often than in the absence of CAD had hypertension, chronic heart failure, diabetes, chronic kidney disease and anemia. Patients with the previous MI had higher incidence of diabetes than those without the previous MI. The frequency of proper cardiovascular pharmacotherapy was insufficient, and to a greater extent in the presence of CAD and the previous MI than in their absence. All-cause mortality was recorded in patients with a combination of AF and CAD more often than in the absence of CAD. All-cause mortality and the incidence of nonfatal myocardial infarction were higher in patients with AF and the previous MI than in those without the previous MI. The presence of CAD and, in particular, the previous MI, was significantly associated with a higher risk of death, as well as a higher risk of developing a combined cardiovascular endpoint.

**Key words:** atrial fibrillation, coronary artery disease, myocardial infarction, outpatient and hospital registries, concomitant diseases, multimorbidity, pharmacotherapy, outcomes, mortality.

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## Introduction

Atrial fibrillation (AF) is the most common heart rhythm disorder, increasing the risk of stroke fivefold and associated with higher mortality [1-3]. Analysis of statistical data shows that the AF incidence is approximately 3% in adults aged 20 and over and is more common in the elderly, as well as in the presence of associated cardiovascular (CVD) and non-cardiac diseases, including arterial hypertension (AH), chronic heart failure (CHF), coronary heart disease (CHD), structural heart abnormalities, obesity, diabetes mellitus (DM) or chronic kidney disease (CKD) [4,5].

Atrial fibrillation is closely associated with coronary heart disease, while the mechanism of pathogenetic influence on the development of AF is due, among other things, to ischemia of atrial cardiomyocytes [2]. The Framingham study found an increase in the prevalence of CHD in patients with newly diagnosed AF [4]. AF in patients with acute coronary syndrome may be associated with an increased risk of ST-segment elevation myocardial infarction [5]. In general, 10-15% of patients with AF undergo percutaneous coronary intervention for CHD [6]. The data of international and Russian studies, which analyzed multimorbidity, pharmacotherapy and outcomes in patients with a combination of atrial fibrillation and CHD, including those with previous myocardial infarction, are limited [7].

Prospective medical registries are the most effective way to study combined CVDs and the quality of drug treatment in real clinical practice [8,9].

Therefore, the actual aim of this study is to assess the structure of comorbid conditions, cardiovascular pharmacotherapy and outcomes in patients with atrial fibrillation and concomitant CHD included in the outpatient and hospital RECVASA registries.

## Materials and methods

Patients with AF were included in 5 cities of the Russian Federation in the following registries: RECVASA (530 people who applied to 3 polyclinics in Ryazan for the period March-May 2012, September-October 2012, and January-February 2013); RECVASA AF-Yaroslavl (404 people who applied to 2 polyclinics in Yaroslavl for the period January-December 2013); RECVASA AF-Moscow (508 people hospitalized at the Federal State Budgetary Institution National Medical Research Center for Preventive Medicine for the period April 2013 – March 2014); RECVASA AF-Tula (1225 people hospitalized at the Tula Regional Clinical Hospital for the period January-December 2013) and RECVASA AF-Kursk (502 patients hospitalized at the Kursk City Clinical Emergency Hospital for the period June 2013–May 2014). 934 (29.5%) of 3169 patients with AF were included in outpatient registries (Ryazan, Yaroslavl) and 2235 (70.5%) were included in hospital registries (Kursk, Moscow, Tula). A more detailed description of the registry study design was published by us earlier [10,11], and we also provided detailed information on the conduct of anticoagulant therapy and the frequency dynamics of its prescription during prospective observation [11].

Inclusion criteria in the study: 1) indication of the AF diagnosis in the outpatient card or in the clinical diagnosis of the disease hospital history; 2) Contacting a polyclinic or hospitalization in a hospital during the above periods of inclusion in the registers. The duration of prospective follow-up (median [Me] and interquartile range [25%; 75%]) of patients was in registers: RECVASA (Ryazan) – 5.8 [3.5; 6.5] years, RECVASA AF-Kursk – 2.2 [1.7; 2.7] years, RECVASA AF-Moscow – 2.0 [1.8; 2.2] years and

RECVASA AF-Yaroslavl – 2.0 [1.8; 2.7] years. Information about the occurrence of events (death, myocardial infarction, acute cerebrovascular accident, hospitalization for CVD) and about the drug therapy carried out at the stage of long-term follow-up was possible to find out by telephone contact or by visiting a doctor within the framework of the above registry studies: in 95.9%; 92.8%; 94.3% and 96.6% of cases, respectively. We assessed the incidence of concomitant CVD and chronic noncardiac diseases, the prescription of drug therapy for CVD, and the outcomes of follow-up.

Methods of descriptive statistics were used for statistical processing of the data. Numerical data are presented as mean and standard deviation ( $M \pm SD$ ) or  $Me$  [25%; 75%]. The statistical significance of differences in numerical data was assessed using the Student's test, and categorical data were assessed using the chi-square test. Differences were considered statistically significant at  $p < 0.05$ . The risk of developing the analyzed events was estimated by the logistic regression method using the creation of the Cox's model and multivariate analysis. The correction for the heterogeneity of the patients' characteristics and their treatment in the regions was applied in multivariate analysis; RECVASA AF-Moscow was taken as the reference register. Statistical data processing was performed using the Statistica 7.0 and Stata 15.0 software.

## Results

A total of 3169 patients were included in 5 AF registers (age was  $70.9 \pm 10.7$  years; 43.1% of men). 2497 patients of them with a combination of AF and CHD (age was  $72.2 \pm 9.9$  years, 43.1% of men;  $CHA_2DS_2$ -VASc –  $4.57 \pm 1.61$ ; HAS-BLED –  $1.60 \pm 0.75$ ), 672 with AF without CHD (age was  $66.0 \pm 12.3$  years; 43.2% of men;  $CHA_2DS_2$ -VASc –  $3.26 \pm 1.67$ ; HAS-BLED –  $1.11 \pm 0.74$ ). Thus, patients with CHD were on average 6.2 years older, had a statistically significantly higher risk of thromboembolic and hemorrhagic complications ( $p < 0.05$ ), while the proportion of men in the compared groups didn't differ significantly ( $p > 0.05$ ).

703 patients with a combination of AF and CHD had a history of myocardial infarction (average age was  $72.3 \pm 9.5$  years; 55.2% of men;  $CHA_2DS_2$ -VASc –  $4.57 \pm 1.61$ ; HAS-BLED –  $1.65 \pm 0.76$ ). 1794 people were in the group of patients with AF and CHD who had not had a myocardial infarction (average age was  $72.2 \pm 10.0$  years; 38.4% of men;  $CHA_2DS_2$ -VASc –  $4.30 \pm 1.50$ ; HAS-BLED –

$1.58 \pm 0.78$ ). Thus, the average age, the risk of thromboembolic and hemorrhagic complications didn't differ significantly in the compared groups but the proportion of men was 1.4 times higher among those who had a myocardial infarction.

The characteristics of combined CVD and concomitant chronic noncardiac diseases among patients with AF and the presence/absence of CHD are presented in Table 1. Patients with a combination of AF and CHD significantly more often than in the absence of CHD were diagnosed with AH, CHF, diabetes mellitus, CKD and anemia. at the same time, only diseases of the digestive system were detected significantly less frequently. Thus, the combined AF with CHD in patients was associated with a greater number of chronic noncardiac diseases compared with individuals without CHD.

Patients with AF in the presence of concomitant CHD significantly more often than in its absence had a permanent form (47.5% and 36.1%;  $p < 0.0001$ ), a persistent form (24.3% and 15.5%;  $p < 0.0001$ ), and newly diagnosed cases of this heart rhythm disorder (22.1% and 3.4%;  $p < 0.0001$ ), less often the paroxysmal form was detected (23.5% and 43.5%;  $p < 0.0001$ ), as well as the absence of the form indication (3.2% and 4.9%;  $p = 0.03$ ). Thus, the later stage of the AF continuum (in almost half of the cases), that is, its permanent form, was more often recorded in patients with more pronounced cardiovascular and noncardiac multimorbidity and with older age. In addition, the frequency of newly diagnosed AF at the inclusion stage in the registry was higher among patients with CHD.

Diabetes mellitus was statistically significantly more often detected as a background pathology among patients with a combination of AF and CHD in the presence of a previous myocardial infarction (27% versus 19.2%,  $p = 0.0008$ ), while the incidence of other cardiovascular and noncardiac diseases (Table 2) didn't differ significantly.

Data on the value of the glomerular filtration rate (GFR) were available in 1114 (35.2%) patients, of whom 361 (32.4%) had this indicator decreased ( $< 60$  ml/min). This indicator was reduced in 250 (34.7%) of 720 patients with a combination of AF, CHD and known GFR. GFR value  $< 60$  ml/min was recorded in 111 out of 394 (28.2%) cases ( $p = 0.03$ ) among people without CHD. Thus, chronic renal failure was more often detected with a combination of AF and CHD. Comparison of groups with and without postinfarction cardiosclerosis (PICS)

**Table 1.** The proportion of people with concomitant CVDs and chronic non-cardiac diseases among patients with AF and the presence/absence of a combination with CHD included in the RECVASA registries

| Diagnosis                        | Patients with AF in a combination with CHD (n=2497) | Patients with AF without a combination of CHD (n=672) | p      |
|----------------------------------|---|---|--------|
| AH, n (%)                        | 2341 (93.8)   | 528 (78.6)  | <0.001 |
| CHF, n (%)                       | 2251 (90.1)   | 344 (51.2)  | <0.001 |
| ACA, n (%)                       | 564 (22.6)  | 138 (20.5)  | 0.260  |
| Diabetes mellitus, n (%)         | 534 (21.4)  | 93 (13.8)   | <0.001 |
| Respiratory diseases, n (%)      | 458 (18.3)  | 104 (15.5)  | 0.080  |
| COPD, n (%)                      | 212 (8.5)   | 55 (8.2)  | 0.800  |
| Bronchial asthma, n (%)          | 85 (3.4)  | 20 (3.0)  | 0.580  |
| Chronic kidney disease, n (%)    | 620 (24.8)  | 119 (17.7)  | 0.001  |
| Anemia, n (%)                    | 176 (7.0)   | 24 (3.6)  | 0.001  |
| Digestive system diseases, n (%) | 1030 (41.2)   | 306 (45.5)  | 0.046  |
| Obesity (in diagnosis), n (%)    | 417 (16.7)  | 115 (17.1)  | 0.300  |

AH – arterial hypertension, CHD – coronary heart disease, CHF – chronic heart failure, ACA – acute cerebrovascular accident, COPD – chronic obstructive pulmonary disease.

among patients with AF and CHD showed that the proportion of people with decreased GFR didn't differ significantly – 35.1% (79 of 225) and 34.5% (171 of 495) cases, respectively ( $p=0.88$ ).

Patients with a combination of AF and CHD with a history of myocardial infarction were significantly more likely to be diagnosed with a paroxysmal form than in the absence of PICS (28.2% and 21.6%;  $p=0.0005$ ) and less often a permanent form (44.0% and 49.0%;  $p=0.02$ ) and newly diagnosed AF (15.8% and 24.6%;  $p<0.0001$ ). There were no significant differences in the frequency of persistent form cases (24.0% and 24.4%;  $p=0.84$ ) and the absence of the AF form indication (3.1% and 3.2%;  $p=0.89$ ) in the compared groups. This arrhythmia was quite often diagnosed for the first time in patients with CHD during a reference visit to the clinic or during a reference hospitalization (in 22.1% of cases), especially in the absence of myocardial infarction history (in 24.6% of cases, that is, in every fourth patient).

Table 3 shows the frequency of prescribing prognostically significant cardiovascular pharmacotherapy in patients with AF in the presence/absence of a combination with CHD. The average frequency of proper drug therapy for

**Table 2.** The proportion of people with concomitant CVDs and chronic non-cardiac diseases among patients with an AF and CHD combination with/without a history of myocardial infarction included in the RECVASA registries

| Diagnosis                        | Patients with AF in a combination with CHD, history of myocardial infarction (n=703) | Patients with AF without a combination of CHD, no history of myocardial infarction (n=1794) | p      |
|----------------------------------|--|---|--------|
| AH, n (%)                        | 657 (93.5)   | 1684 (93.9)   | 0.700  |
| CHF, n (%)                       | 645 (91.7)   | 1607 (89.5)   | 0.100  |
| ACA, n (%)                       | 168 (23.9)   | 396 (22.1)  | 0.330  |
| Diabetes mellitus, n (%)         | 190 (27.0)   | 344 (19.2)  | <0.001 |
| Respiratory diseases, n (%)      | 131 (18.6)   | 328 (18.3)  | 0.840  |
| COPD, n (%)                      | 64 (9.1)   | 148 (8.2)   | 0.490  |
| Bronchial asthma, n (%)          | 22 (3.3)   | 63 (3.5)  | 0.640  |
| Chronic kidney disease, n (%)    | 170 (24.2)   | 450 (25.1)  | 0.630  |
| Anemia, n (%)                    | 54 (7.7)   | 122 (6.8)   | 0.440  |
| Digestive system diseases, n (%) | 281 (40.0)   | 750 (41.8)  | 0.400  |
| Obesity (in diagnosis), n (%)    | 108 (15.4)   | 309 (17.2)  | 0.260  |

AH – arterial hypertension, CHD – coronary heart disease, CHF – heart failure, ACA – acute cerebrovascular accident, COPD – chronic obstructive pulmonary disease.

CHD was less in the presence of an AF and CHD combination compared with cases of the absence of chronic coronary pathology clinical manifestations (67.8%, compared to 74.5%), mainly due to the more rare prescription of anticoagulants (by 1.7 times).

The proportion of patients who were prescribed antiplatelet agents instead of anticoagulants was 39.5% (1252 out of 3169), and it was higher than the proportion of patients prescribed proper anticoagulant therapy – 30.8% (976 out of 3169). At the same time, the proportion of prescribing antiplatelet agents in the absence of prescribing anticoagulants among patients with CHD was 66.9% (1670 out of 2497) and was 2.5 times higher than among patients with AF without coronary heart disease – 26.4% (178 out of 673),  $p<0.0001$ . The proportion of prescribing antiplatelet agents instead of the necessary anticoagulant therapy among patients with a history of myocardial infarction was 60% (422 of 703) and was 1.3 times higher than among patients with AF without a previous myocardial infarction – 46.5% (830 of 1794),  $p<0.0001$ .

Table 4 shows the frequency of prescribing prognostically significant pharmacotherapy for CVD in patients with AF

**Table 3.** The frequency of prescribing prognostically significant pharmacotherapy for CVD in patients with AF in the presence/absence of a combination with CHD (data from the RECVASA registries)

| Drug therapy and indications                            | Patients with AF in a combination with CHD (n=2497) | Patients with AF without a combination of CHD (n=672) | p      |
|---|---|---|--------|
| Antihypertensive therapy for AH                         | 94.0% (2200 of 2341)                                | 93.0% (491 of 528)                                    | 0.400  |
| ACEi/ARBs for CHF                                       | 84.4% (1900 of 2251)                                | 83.4% (287 of 344)                                    | 0.640  |
| ACEi/ARBs for PICS                                      | 85.5% (601 of 703)                                  | –   | –      |
| Beta-blockers for CHF                                   | 64.4% (1449 of 2251)                                | 62.8% (216 of 344)                                    | 0.570  |
| Beta-blockers for PICS                                  | 74.0% (520 of 703)                                  | –   | –      |
| Statins for CVD   | 56.3% (1406 of 2497)                                | –   | –      |
| Statins in case of cerebral stroke                      | 58.0% (327 of 564)                                  | 63.8% (88 of 138)                                     | 0.220  |
| Anticoagulants  | 39.1% (976 of 2497)                                 | 66.2% (445 of 672)                                    | <0.001 |
| ACEi in case of cerebral stroke                         | 65.4% (369 of 564)                                  | 61.6% (85 of 138)                                     | 0.400  |
| Average frequency of compliance with mandatory readings | 67.8% (9748 of 14371)                               | 74.5% (1612 of 2164)                                  | –      |

AH – arterial hypertension, CHD – coronary heart disease, PICS – postinfarction cardiosclerosis, CHF – chronic heart failure, ACEi – angiotensin-converting enzyme inhibitors, ARB – angiotensin receptor blocker.

in combination with CHD in the presence/absence of previous myocardial infarction. The average frequency of prescribing proper drug therapy for CVD was more often in patients with an AF and CHD combination in the presence of a previous myocardial infarction (74.3% versus 63.3%), including angiotensin-converting enzyme inhibitors (ACEi)/angiotensin II receptor blockers (ARB), beta-blockers for CHF, statins and anticoagulants were more often prescribed to patients.

Based on the data of prospective observation, the analysis of the frequency of fatal and non-fatal events in patients with AF in the presence/absence of a combination with CHD was carried out (Table 5). All-cause death (by 2.9 times), the development of nonfatal cerebral stroke (by 3.1 times) and hospitalization for CVD (by 1.7 times) were significantly more often recorded in patients with a combination of AF and CHD compared with patients without CHD.

Patients with PICS during long-term prospective follow-up (Table 6) had a higher all-cause mortality rate (by 1.4 times) and the incidence of nonfatal myocardial infarction (by 3.3 times) than those without a history of myocardial infarction (Table 6). According to multivariate analysis, taking into account age and gender factors (Tables 7 and 8), the presence of CHD and, in particular, PICS, was significantly associated with a higher risk of death (risk ratio [RR]=1.58; 95% confidence interval [CI] was 1.33-1.88;  $p<0.001$  and  $RR=1.59$ ; 95% CI was 1.33-1.90;  $p<0.001$ ), as well as with a higher risk of developing a combined cardiovascular endpoint ( $RR=1.88$ ;

95% CI was 1.17-3.00;  $p<0.001$  and  $RR=1.75$ ; 95% CI was 1.44-2.12;  $p<0.001$ , respectively).

## Discussion

According to the results of the present study, CHD was diagnosed in 78.8% of patients from AF registers, and 28.2% of them had had myocardial infarction before. According to the data of AF international registries, the incidence of CHD is 14-45%, [12-14], which is significantly less than our data. The AF incidence in acute coronary syndrome (ACS) ranges from 2 to 23% [15]. According to the data of the RECVASA outpatient register of cardiovascular diseases, a simultaneous combination of AF, AH, CHD and CHF was detected in 93.2% of patients with AF. In this group of patients, the highest incidence of myocardial infarction and cerebral stroke in the anamnesis was revealed (21.3% and 16.8%, respectively) [10]. According to the Euro Heart Survey, Cardiotens 99, PREFER in AF registry, the proportion of patients with myocardial infarction among patients with AF was similar and amounted to 13-20% [14,16,17].

AH, CHF, diabetes mellitus, CKD and anemia were diagnosed in patients with an AF and CHD combination significantly more often than in the absence of CHD. That is, the presence of an AF and CHD combination in patients was associated with a greater number of chronic non-cardiac diseases compared with those without CHD, while the proportion of people with diabetes mellitus and CKD was comparable to the results obtained in the international registries ATRIUM and Euro Heart Survey [13, 14].



**Table 4.** The frequency of prescribing prognostically significant pharmacotherapy for CVD in patients with AF in a combination with CHD in the presence/absence of previous myocardial infarction (data from the RECVASA registries)

| Drug therapy and indications                            | Patients with AF in a combination with CHD, history of myocardial infarction (n=703) | Patients with AF without a combination of CHD, no history of myocardial infarction (n=1794) | p      |
|---|--|---|--------|
| Antihypertensive therapy for AH                         | 95.3% (626 of 657)   | 93.5% (1574 of 1684)  | 0.100  |
| ACEi/ARBs for CHF                                       | 84.6% (556 of 657)   | 79.8% (1344 of 1684)  | 0.007  |
| ACEi/ARBs for PICS                                      | 85.5% (601 of 703)   | –   | –      |
| Beta-blockers for CHF                                   | 74.6% (481 of 645)   | 60.3% (969 of 1607)   | <0.001 |
| Beta-blockers for PICS                                  | 74.0% (520 of 703)   | –   | –      |
| Statins   | 68.8% (484 of 703)   | 51.4% (922 of 1794)   | <0.001 |
| Statins in case of cerebral stroke                      | 60.7% (102 of 168)   | 56.8% (225 of 396)  | 0.390  |
| Anticoagulants  | 44.0% (309 of 703)   | 37.2% (667 of 1794)   | 0.002  |
| ACEi in case of cerebral stroke                         | 69.6% (117 of 168)   | 63.6% (252 of 396)  | 0.170  |
| Average frequency of compliance with mandatory readings | 74.3% (3796 of 5107)   | 63.3% (5953 of 9355)  | –      |

AH – arterial hypertension, CHD – coronary heart disease, PICS – postinfarction cardiosclerosis, CHF – chronic heart failure, ACE inhibitors – angiotensin-converting enzyme inhibitors, ARB – angiotensin receptor blocker.

**Table 5.** The frequency of fatal and non-fatal events according to the prospective observation data of patients with AF in the presence/absence of a combination with CHD

| Events                                 | Patients with AF in a combination with CHD (n=2497) | Patients with AF without a combination of CHD (n=672) | p      |
|--|---|---|--------|
| All-cause mortality, n (%)             | 580 (23.2)  | 53 (7.9)  | <0.001 |
| Non-fatal myocardial infarction, n (%) | 116 (4.6)   | –   | –      |
| Non-fatal cerebral stroke, n (%)       | 144 (5.8)   | 13 (1.9)  | <0.001 |
| Hospitalization for CVD, n (%)         | 1101 (22.9)   | 91 (13.5)   | <0.001 |

AF – atrial fibrillation, CHD – coronary heart disease, CVD – cardiovascular diseases

**Table 6.** The frequency of fatal and non-fatal events according to the prospective observation data of patients with an AF and CHD combination in the presence/absence of previous myocardial infarction

| Events                                 | Patients with AF in a combination with CHD, history of myocardial infarction (n=703) | Patients with AF without a combination of CHD, no history of myocardial infarction (n=1794) | p      |
|--|--|---|--------|
| All-cause mortality, n (%)             | 204 (29.0)   | 376 (21.0)  | <0.001 |
| Non-fatal myocardial infarction, n (%) | 51 (7.3)   | 40 (2.2)  | <0.001 |
| Non-fatal cerebral stroke, n (%)       | 46 (6.5)   | 98 (5.5)  | 0.300  |
| Hospitalization for CVD, n (%)         | 177 (25.2)   | 396 (22.1)  | 0.100  |

AF – atrial fibrillation, CHD – coronary heart disease, CVD – cardiovascular diseases

The present study showed that patients with AF in the presence of CHD significantly more often than in the absence of CHD had its permanent form, persistent form and newly diagnosed cases of this heart rhythm disturbance, and the paroxysmal form was detected less often. Newly diagnosed AF was diagnosed significantly more often than in the absence of PICS in patients with an AF and CHD combination with a history of my-

ocardial infarction. The clinical features of patients with paroxysmal and non-paroxysmal AF vary greatly, which may affect treatment and prognosis. According to the Realise AF registry, an increase in the incidence of cardiovascular and noncardiac diseases (CHD, CHF, chronic obstructive pulmonary disease, cerebrovascular diseases, and thromboembolic complications) was observed as AF progressed from paroxysmal to permanent [18]. Ac-

**Table 7. Assessment of the association of coronary heart disease factor in patients with atrial fibrillation with the risk of death and the development of a combined cardiovascular endpoint\***

| Factor                      | Risk of death from all causes (RR, 95% CI, p)<br>1037 events | Risk of combined cardiovascular endpoint<br>(RR, 95% CI, p) 530 events |
|-----------------------------|--|--|
| Age, for 1 year             | 2.75 (2.01-3.77)<br>p<0.001                                  | 2.76 (1.65-4.51)<br>p<0.001  |
| Gender (female – reference) | 2.17 (1.43-3.16)<br>p<0.001                                  | 3.96 (2.11-7.45)<br>p<0.001  |
| CHD                         | 1.19 (0.94-1.50)<br>p=0.15                                   | 1.53 (1.05-2.35)<br>p=0.045  |

\*combined cardiovascular endpoint (death from CVD, non-fatal myocardial infarction and cerebral stroke, surgery for CVD)  
CVD – cardiovascular diseases, RR – risk ratio, CI – confidence interval, CHD – coronary heart disease.

**Table 8. Assessment of the association of previous myocardial infarction factor in patients with an AF and CHD combination with the risk of death and the development of a combined cardiovascular endpoint\***

| Factor                           | Risk of death from all causes (RR, 95% CI, p)<br>1037 events | Risk of combined cardiovascular endpoint<br>(RR, 95% CI, p) 530 events |
|----------------------------------|--|--|
| Age, for 1 year                  | 2.75 (2.01-3.77)<br>p<0.001                                  | 2.76 (1.65-4.51)<br>p<0.001  |
| Gender (female - reference)      | 2.17 (1.43-3.16)<br>p<0.001                                  | 3.96 (2.11-7.45)<br>p<0.001  |
| History of myocardial infarction | 1.19 (0.94-1.50)<br>p=0.150                                  | 1.53 (1.05-2.35)<br>p=0.045  |

\* - combined cardiovascular endpoint (death from CVD, non-fatal myocardial infarction and cerebral stroke, surgery for CVD)  
CVD – cardiovascular diseases, RR – risk ratio, CI – confidence interval, CHD – coronary heart disease.

cording to the results of a prospective population study conducted in Rotterdam, the risk of newly registered AF in patients with myocardial infarction increases by 60-77% [19]. Several mechanisms may explain the association of previous myocardial infarction with AF development. Atrial dilation due to myocardial infarction can lead to an increase in atrial pressure, with catecholamines released in response to atrial dilatation, which increases the AF risk [20]. It was also suggested that AF may develop secondary due to left ventricular dysfunction and hemodynamic disturbances after myocardial infarction. Finally, atrial ischemia can create both triggers for the AF onset and a substrate for its subsequent maintenance [21].

The frequency of prescribing prognostically significant cardiovascular pharmacotherapy for CVD in patients with AF was insufficient, and to a greater extent in the presence of CHD (67.8%) compared to 74.5% in its absence, as well as in the presence of PICS (74.3%) compared to 63.3% in its absence. These data are consistent with the results obtained in the prospective registry RECVASA-CLINIC, where patients with AF in combination with CHD, hypertension, and CHF at the outpatient stage were not

often prescribed beta-blockers, ACEi/ARB, statins and anticoagulants affecting on the prognosis [7], as well as with the data obtained in the REGION registry, which analyzed patients with AF and acute cerebrovascular accident, with myocardial infarction and without a myocardial infarction history. And the average frequency of prescribing proper drug therapy for CVD was more often in the presence of a previous myocardial infarction (46.6% versus 38.9%) [22].

According to clinical guidelines for stable CHD and AF, oral anticoagulant therapy is recommended for patients with a combination of these diagnoses in order to reduce the risk of ischemic stroke and other thromboembolic complications [2,23]. Anticoagulants in AF patients have been shown to be superior to aspirin monotherapy or clopidogrel-based dual antiplatelet therapy for the prevention of stroke. Antithrombotic therapy in the form of monotherapy with oral anticoagulants, rather than a combination of oral anticoagulants with antiplatelet agents and not monotherapy with antiplatelet agents, is recommended for patients with AF and stable CHD in the absence of a history of ACS and/or coronary intervention in the previous 12 months [23-25].

According to the results of this study, the proportion of patients who were prescribed antiplatelet agents instead of the proper prescription of anticoagulants was 39.5% and turned out to be more than the proportion of prescribing the necessary anticoagulant therapy – 30.8%. At the same time, the proportion of prescribing antiplatelet agents in the absence of prescribing anticoagulants was 2.5 times higher among patients with CHD than among patients with AF without CHD. And the proportion of prescribing antiplatelet agents instead of properly prescribing anticoagulants was 60% among patients with myocardial infarction, which is 1.3 times more than among patients with AF without a previous myocardial infarction – 46.5%.

The frequency of prescribing anticoagulants to patients with AF is comparable to the data of Russian registries (16% in the RECVASA AF outpatient registries, 40.2% in the RECVASA AF hospital registries, 20.7% in the REGION register) [11,26]. According to the data of the atrial fibrillation registers ORBIT-AF I, ORBIT-AF II and GARFIELD-AF, in Western Europe the frequency of prescribing anticoagulants to patients with AF is significantly higher and amounts to 60-80% [27]. At the same time, observational studies have shown that patients with AF and ACS are less likely to receive appropriate antithrombotic therapy [28] and are more likely to experience adverse outcomes [29] than patients with ACS without AF. In the BALKAN-AF registry, which included 2,712 AF patients, it was shown that antithrombotic therapy was suboptimal in multimorbid patients with AF, and 18% of multimorbid patients didn't receive anticoagulants, while the presence of CHD and myocardial infarction were independent predictors of the absence of oral anticoagulants prescription in multimorbid patients with newly diagnosed AF [30].

Our study revealed that all-cause death (by 2.9 times) and non-fatal myocardial infarction (by 3.1 times) were more often recorded in patients with a combination of AF and CHD than in the absence of CHD. All-cause mortality (by 1.4 times) and the incidence of nonfatal myocardial infarction (by 3.3 times) were higher in patients with AF and PICS during the follow-up period than in those without PICS. At the same time, according to multivariate analysis, taking into account age and gender factors, the presence of CHD and, in particular, PICS, was associated with a higher risk of death (by 1.6 times) and with a higher risk of developing a combined cardiovascular endpoint (by

1.9 and 1.7 times). According to our previously published data, 61.8% of all deaths accounted for deaths from cardiovascular causes in the analyzed cohort of AF patients [31].

The RE-LY study analyzed the causes of death in 18,113 AF patients. 37.4% of all deaths accounted for deaths from cardiovascular causes. The most significant independent predictors of cardiac death in this population were heart failure (RR=3.02;  $p<0.0001$ ) and previous myocardial infarction (RR=2.05;  $p<0.0001$ ) [32]. Several other studies have also shown an association of myocardial infarction with an increased risk of death in AF patients [33, 34]. According to the registry, which included 6,000 patients with acute myocardial infarction, patients admitted with acute myocardial infarction and AF had a higher risk of acute stroke, nosocomial death, and readmission within 30 days [35]. Also, T. Pilgrim et al. showed that AF increases the risk of ischemic and hemorrhagic stroke among patients with stable CHD who underwent percutaneous coronary intervention [36].

## Conclusion

CHD was diagnosed in 78.8% of patients from AF registers in 5 regions of Russia, and 28.2% of them had had myocardial infarction before. The presence of an AF and CHD combination in patients was associated with a higher frequency of diagnosing AH, CHF, diabetes mellitus, CKD, and anemia. Chronic renal failure, characterized by a decrease in GFR, was more often detected with an AF and CHD combination. The frequency of proper cardiovascular pharmacotherapy was insufficient, and to a greater extent in the presence of CHD than in its absence, as well as in the presence of PICS than in its absence. All-cause death and nonfatal cerebral stroke were more often recorded in patients with an AF and CHD combination than in the absence of CHD. All-cause mortality and the incidence of nonfatal myocardial infarction were higher in patients with AF and previous myocardial infarction during the follow-up period than in those without a myocardial infarction history. According to multivariate analysis, taking into account age and gender factors, the presence of CHD and, in particular, PICS, was significantly associated with a higher risk of death, as well as a higher risk of developing events corresponding to the combined cardiovascular endpoint.



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