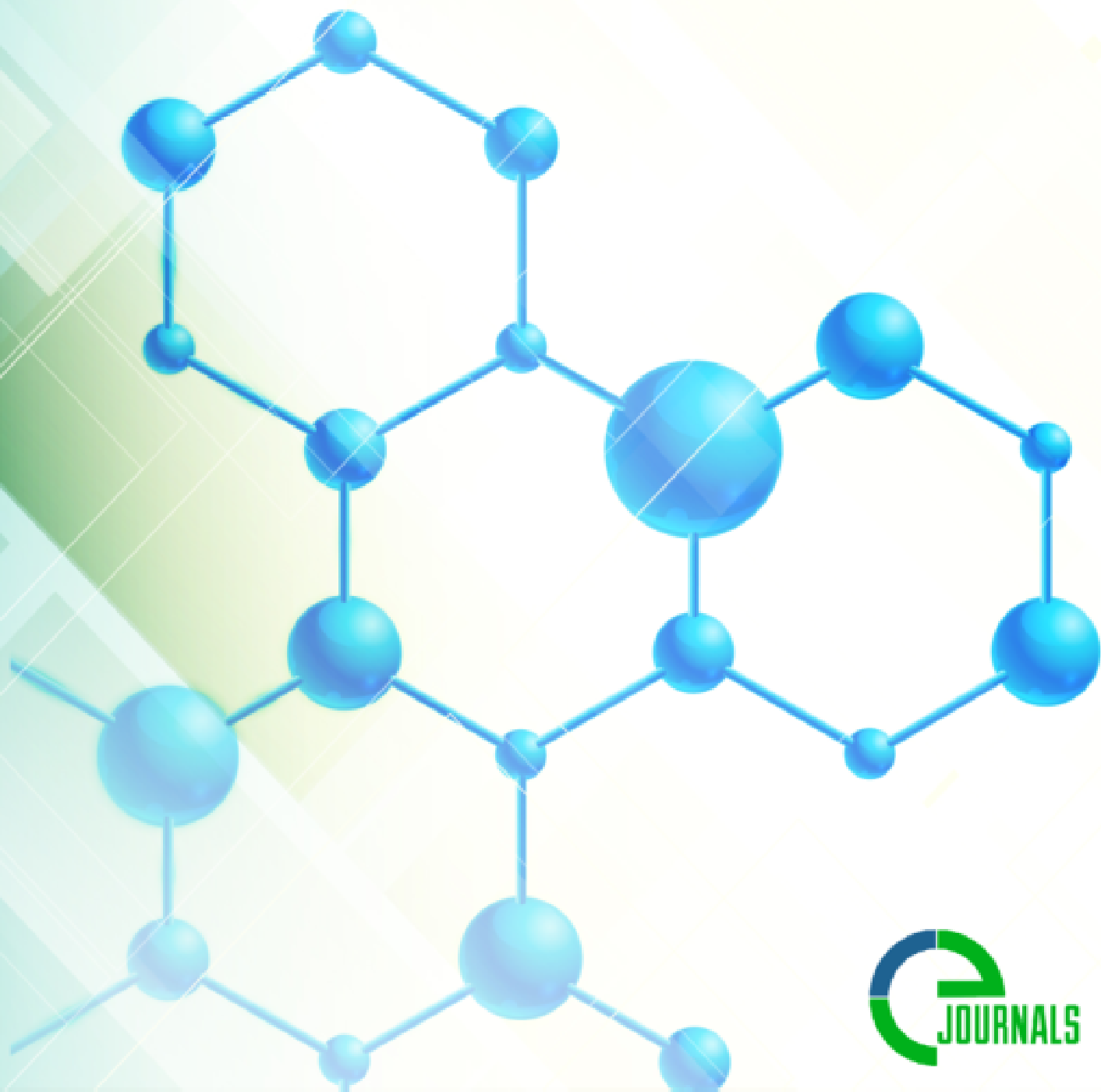


EUROPEAN JOURNAL OF  
**MOLECULAR MEDICINE**



**European Journal of Molecular medicine**

**Volume 2, No.1, January 2022**

**Internet address:** <http://ejournals.id/index.php/EJMM/issue/archive>

**E-mail:** [info@ejournals.id](mailto:info@ejournals.id)

Published by ejournals PVT LTD

DOI prefix: 10.52325

Issued Bimonthly

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## THE CLINICAL COURSE OF ATRIAL FIBRILLATION IN PATIENTS WITH CORONARY HEART DISEASE

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*Abstract: Atrial fibrillation (AF) is one of the most common cardiac arrhythmias, with a frequency in the general population of 2% and continues to increase [1]. AF affects the quality of life of patients and reduces life expectancy. AF is believed to be an independent risk factor for cardiovascular disease. According to the latest recommendations for the diagnosis and treatment of AF, there are 5 types of arrhythmias: first detected, paroxysmal, persistent, prolonged persistent and permanent [1]. The majority of patients with AF progresses to a persistent or permanent form, leading to a worsening of the clinical picture of patients and their prognosis.*

*Key words: Coronary heart disease, persistent form of atrial fibrillation, progression factors.*

The factors leading to the progression of AF can be divided into "established" and "new". The "established" more confirmed are arterial hypertension (AH), chronic heart failure (CHF), damage to the heart valves and age. And the "new" and less studied factors of AF progression include ischemic heart disease (IHD), obesity, diabetes mellitus, chronic kidney disease, sleep apnea, chronic obstructive pulmonary disease and hereditary predisposition [2, 3]. IHD affects more than 20% of patients with AF [3]. AF in patients with coronary artery disease increases the risk of thromboembolic complications that contribute to the progression of CHF. At the same time, a controversial question is posed: does uncomplicated coronary artery disease predispose to the onset of AF and whether the severity of coronary atherosclerosis affects the course of arrhythmia [3]. According to the latest data in the medical literature, there are practically no clinical studies aimed at studying the factors of arrhythmia progression in patients with coronary artery disease. In this connection, the study of the clinical course of AF in patients with coronary artery disease is relevant.

**Purpose of the study:** to study the features of the clinical course of AF in patients with coronary artery disease.

### **Material and methods**

A total of 112 patients with coronary artery disease with persistent AF at the age of 51 to 73 years (mean age  $67.44 \pm 3.3$  years) were examined. The presence of AF and the diagnosis of ischemic heart disease were confirmed on the basis of characteristic complaints, medical history, physical examinations, and instrumental examinations such as ECG and ECHOKG registration. The exclusion criteria were cardiogenic shock; acute coronary syndrome; congenital and acquired heart defects; inflammatory heart disease; obesity of the III degree and dysfunction of the thyroid gland. The structural and functional state of the heart was studied by echocardiography on a Sonoscape SSI 5000 device (China) with a 2.4 MHz transducer. The average value of three consecutive heart cycles was calculated. The standard positions of the parasternal and apical approaches were used. The state of local contractility of the left and right ventricles was studied by 17-segment division of the left and right ventricles. The regional ejection fraction (EF) ranged from 25% -kinetic, EF 25-50% - hypokinetic, and EF more than 50% - normokinetic. After fixing the registrations of the initial hemodynamic parameters, the local contractility parameters were re-

diagnosed under the conditions of an acute drug test with nitrate - 30 minutes after sublingual administration of nitroglycerin alone. The average value of three consecutive heart cycles was calculated. The standard positions of the parasternal and apical approaches were used. The state of local contractility of the left and right ventricles was studied by 17-segment division of the left and right ventricles. The regional ejection fraction (EF) ranged from 25% -kinetic, EF 25-50% - hypokinetic, and EF more than 50% - normokinetic. After fixing the registrations of the initial hemodynamic parameters, the local contractility parameters were re-diagnosed under the conditions of an acute drug test with nitrate - 30 minutes after sublingual administration of nitroglycerin alone. Clinical features of AF were carried out on the basis of calculating the number of arrhythmia attacks for 3 months, as well as the results of 24-hour Holter ECG monitoring. Improvement of arrhythmia was considered as an increase in the frequency of arrhythmia paroxysms over the last 3 months, the appearance of long-term persistent attacks or a permanent form of AF. Over 2 years of follow-up, 64 (57.2%) patients (group 1) did not observe an increase in the frequency and duration of AF attacks, arrhythmia progression was observed in 48 (42.8%) patients (group 2) out of 112 (100 %) of patients included in the study. The average value of arrhythmia progression was 6.7% per year.

All patients included in the study had an arrhythmic history from 1 to 8 years. With AF progression, the mean arrhythmia duration was  $5.82 \pm 2.35$  years, and in patients without signs of progression, it was  $4.3 \pm 1.71$  years ( $p < 0.05$ ). In the history of patients with progression of AF, myocardial infarction and CHF were more common than in patients without progression of arrhythmia. Acute cerebrovascular accident (ACVI) in history in patients of the 1st group was noted in 3 (6%), and in patients of the 2nd group in 7 (20.9%) ( $p < 0.05$ ). According to echocardiography, the ejection fraction (EF) of the left ventricle (LV) in all patients was higher than 44%. In the 1st group of patients, the average LVEF was  $61.23 \pm 6.24\%$ , and in the 2nd group -  $48.47 \pm 8.4\%$ . The end-systolic volume (EDV) of the LV was greater in patients with progression of AF than in patients without progression of AF. Mitral regurgitation was diagnosed in 47% of patients in group 2 and 28% of patients in group 1 ( $p < 0.05$ ). In patients with progressive AF, a greater number of zones of hypokinesis and akinesis were recorded than in patients without progression of arrhythmia (Table 2).

Table 1. Clinical characteristics of patients

		1 group		g r o u p
Number of patients (%)	112(100)	64(57,2)	48(42,8)	
Average age, (M ± m)	66,4±3,3	65,5±4,23	67,52±5,19 нд	
Men, n (%)	40 (35,7)	20 (31,3)	20 (41,7)	
Women, n (%)	72 (64,3)	44 (68,8)	28 (58,3)	
Arterial hypertension, n (%):				
I stage	2 (1,9)	1 (1,7)	1 (2,1)	
II stage	36 (33,6)	20 (33,3)	16 (34,0)	
III stage	62 (57,9)	37 (61,7)	25 (53,2)	
Duration AF, years (M ± m)	5,96 ± 1,52	4,6 ± 1,74	7,84 ± 2,85 un.	
Ischemic heart disease, n (%):				
angina pectoris FC II	32 (28,2)	18 (27,4)	14 (29,2)	
angina pectoris FC III	29 (23,6)	15 (22,6)	14 (25)	
History of myocardial infarction, n (%)	25 (22)	10 (15,6)	15 (31,3)	
History of ACVA, n (%)	10 (16,2)	3 (6)	7(20,9)	
Body mass index, kg/m2 (M ± m)	26,12 ± 1,98	26,82 ± 2,4	25,27 ± 3,01 un.	
Chronic heart failure (NYHA), n (%):	65 (58)	33 (51,5)	32 (67)	

Index. Patients included in the study Group 1 Group 2

Note. ACVA — acute cerebrovascular accident; FC — functional class; un. - unreliable.

Table 2. Echocardiography parameters at the time of enrollment of patients into the study

Echocardiography parameters	Group 1	Group 2
EF LV,% (M ± T)	61,23 ± 6,24	48,47 ± 8,4 нд
EDV, ml (M ± T)	118,32 ± 16,3	133,42 ± 21,6нд
ESV, ml (M ± T)	43,51 ± 10,32	61,38 ± 17,19нд
BWT LV (M ± T)	1,10 ± 0,099	1,10 ± 0,06нд
AST (M ± T)	1,2 ± 0,099	1,17 ± 0,07нд
The size LA, sm (M ± T)	4,3 ± 0,5	4,8 ± 0,1нд
Decrease in local contractility of the LV myocardium, n (%):		
number of akinesis zones	17 (37)	24 (50)
number of hypokinesis zones	53 (84,1)	38 (79,2)
Mitral regurgitation, (%)	7 (28)	8 (47)

Note. EDV - end diastolic volume; ESV - end systolic volume; BWT - back wall thickness; TIS — the thickness of the interventricular septum; LA - left atrium; un. - unreliable.

The presence of a zone of hypokinesis and segments of hypokinesis was detected both in patients with postinfarction cardiosclerosis and in patients without a history of myocardial infarction. In patients without progression of AF, the number of akinesis zones was noticeably less than in patients with progression of arrhythmia. All patients with a history of myocardial infarction had akinesis zones. In order to determine the reserve capacity of the myocardium, all patients underwent an acute drug test with nitroglycerin. In the 1st group of patients, after taking nitrate, there was a positive dynamics of local LV contractility in the form of a decrease in the number of hypokinesis zones, a significant increase in the number of normokinetic segments, and the zones of akinetic segments did not clearly change. In the 2nd group of patients taking nitrate, no significant changes in the local contractile function of the LV myocardium were revealed: the number of normokinesis zones slightly increased, the number of hypokinesis zones slightly decreased, and the number of akinetic segments remained unchanged.

In group 2, the absence of significant changes in local myocardial contractility during an acute drug test with nitroglycerin indicates severe sclerotic changes in the LV myocardium in patients with coronary artery disease, contributing to the transition of paroxysmal AF to long-term persistent or permanent.



Over the past 5 years, a large number of scientific studies have been carried out in which it has been proven that AF has a clear pattern of natural course from a stage that does not have clinical manifestations to the final stage, which is irreversible arrhythmia [4-6]. A retrospective analysis of the Euro Heart Survey (2010), which included patients with paroxysmal AF, identifying the most important factors of AF progression and substantiating the risk scale for the transition of paroxysmal AF to permanent form [5]. The progression of arrhythmia was associated with the presence of CHF, age (over 75 years), previous thromboembolism or stroke, chronic obstructive pulmonary disease and hypertension. The study of statistical analysis made it possible to derive the formula for the HATCH scale; a value on this scale in the range of 6-7 determines the high probability (more than 50% of cases) of the transition of paroxysmal AF to a persistent or long-term persistent form within the next year [4]. In the USA, the largest retrospective analysis was carried out to study the factors of AF progression, which is based on the registration of a database of patients with AF (Outcomes Registry for Better Informed Treatment of AF; ORBIT-AF) [5]. 6235 patients with paroxysmal and persistent forms of AF were included in the study; the duration of the follow-up was 18 months. The authors formulated the following conclusions: in more than 20% of patients with paroxysmal AF, after 1.5 years of follow-up, a transition to a long-term persistent or permanent form is revealed. The main factors in the development of AF are the age of the patients, high ventricular rate and CHF. It is important to note that the HATCH scale is not very informative in determining the risk of evolution of the clinical course of AF [5]. At the time of the study, with prospective observation for  $48 \pm 3$  months, the progression of arrhythmia was observed in 48 (42.8%) patients with coronary artery disease with paroxysmal AF. The transformation of paroxysmal AF into more stable forms occurred in patients with a longer arrhythmic history and a severe stage of CHF. In the group of patients with progression of arrhythmia, the transferred myocardial infarction and stroke were significantly more often detected. According to the parameters of the study of echocardiography, it was found that the progression of arrhythmia was observed in patients with severe mitral regurgitation, higher volumetric parameters of the left ventricle and lower figures of left ventricular ejection fraction. The same results were obtained in the work of Korean scientists [6]. 434 patients with paroxysmal AF (mean age  $71.7 \pm 10.7$  years, 60% men) were included in the study. After  $72.7 \pm 58.3$  months of observation, 168 (38.7%) patients underwent a transformation of paroxysmal AF into a persistent or permanent form. Considering many factors, the analysis revealed that independent factors of AF progression throughout the study were the presence of atrial arrhythmia, LVEF, LV hypertrophy, LA and LV dilatation, severe mitral regurgitation, patient age and body mass index [6]. If arrhythmias lasted more than 48 hours and there was no adequate anticoagulant therapy during the last 3 weeks, echocardiography was performed in all patients before the restoration of sinus rhythm using electrical cardioversion (EC) in order to exclude an intra-atrial thrombus and study the size of the left atrium [7]. During the study period, in patients with AF progression, we found pronounced changes in the local contractility of the LV myocardium in the form of a significant increase in the number of akinesis zones and a decrease in the number of normokinesis zones as compared to those in patients in whom the evolution of the course of arrhythmia was not observed. At the time of the test with nitroglycerin in patients of the 1st group, there was an improvement in the local contractility of the LV myocardium, there was a significant increase in the zones of normokinetic segments and a decrease in the number of zones of hypokinesis. The presence of reversibility of areas of hypokinesis during an acute test with nitroglycerin indicates the presence of zones of myocardial hibernation in patients with coronary artery disease. When taking nitroglycerin, the absence of changes in local contractility in patients of group 2 indicates severe sclerotic changes in the LV myocardium, which determines the remodeling of the heart chambers and the progression of arrhythmia.



**Conclusions**

1. During the study, 42.8% of patients with ischemic heart disease with paroxysmal atrial fibrillation showed progression of arrhythmia to persistent or permanent form. The mean progression of atrial fibrillation was 6.7% per year.

2. In patients with ischemic heart disease, predictors of atrial fibrillation progression are past myocardial infarction, chronic heart failure, severe mitral regurgitation and irreversible changes in the local contractility of the left ventricular myocardium.

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