



## COGNITIVE SYMPTOMS OF CHRONIC DISORDERS OF CEREBRAL CIRCULATION IN PATIENTS WITH ATRIAL FIBRILLATION

STADNIK S.N.

Military Medical Clinical Center of Western region, Lviv, Ukraine

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### ABSTRACT

*Atrial fibrillation is a heart rhythm disorder, accompanied by numerous systemic disorders. One of them accounting for changes in the central nervous system is of great importance. Reduction of cardiac output and contractile function of the heart cause a deterioration of cerebral blood flow, thus contributing to the formation and progression of cognitive disorders that subsequently can lead to dementia. The objective of this study was to investigate clinical manifestations of chronic cerebrovascular pathology in patients with different clinical forms of atrial fibrillation based on neuropsychological studies.*

*Eighty two patients with atrial fibrillation nonvalvular etiology, developed due to coronary heart disease, were examined. The comparison group consisted of 30 patients with ischemic heart disease without any cardiac rhythm and conduction. Patients in both groups underwent a computed tomography examination of the brain.*

*The study established that cognitive disorders in patients with atrial fibrillation were manifested in attention deficit, reduced rate of speech and mental activity, impaired visual-spatial functions and secondary memory disorders. The permanent form of atrial fibrillation showed accelerated decrease in the speed of psychomotor reactions, visual-spatial disorders and memory loss, whereas deterioration of cognitive functions occurs regardless of age, duration of hypertension, and predictors of dyslipidemic disorders.*

*The presence of atrial fibrillation is associated with a higher incidence of diffuse lesions of the white matter of the brain. The most pronounced changes in patients with atrial fibrillation are detected in the periventricular matter and perivascular spaces. The progression of diffuse changes of the white matter of the brain associated with the increase of memory disorders, attention and mental speed.*

*Thus, early manifestations of chronic disorders of cerebral circulation in patients with atrial fibrillation in the absence of severe focal neurological symptoms may be mild cognitive disorders, whose identification is necessary due to the increased risk of progression to the stage of severe cognitive deficits.*

**KEYWORDS:** atrial fibrillation, cognitive disorders, leukoaraiosis.

### INTRODUCTION

Atrial fibrillation (AF) is one of the most common arrhythmia, which is considered an epidemic of the twenty-first century. A significant increase in the incidence of AF has occurred over the last decades. Thus, in Framingham study age-regulated prevalence of AF for the 22-year period increased

from 3.2 (1968-1970) to 9.1% (1987-1989) in men and from 2.8 to 4.7% in women, respectively. Its frequency increases with age and reaches 3.8% among people over 60 and 9% after 80 [Puccio D *et al.*, 2009; Alekhine AN *et al.*, 2011].

The prevalence of cognitive disorders (CD) is extremely high, and in recent years there has been a tendency towards steady growth. However, despite this, in some cases, there is an underestimation of some risk factors in the development of CD. Delayed diagnosis of the early stages of CD and, accordingly, the absence of adequate therapy

### ADDRESS FOR CORRESPONDENCE:

Department of Intensive Care Unit, Cardiology Clinic  
at the Military Medical Clinical Center  
7/59 Polubotka St., Lviv 79066, Lviv, Ukraine  
Tel.: (+380 67) 337-70-67  
Email: depor-ss@yandex.ru

lead to their further progression [Zakharov VV, 2003; Yahno NN et al., 2005; Starchina UA, 2006]. Special attention should obviously be given to patients with cardiac pathology.

The most studied are CD with arterial hypertension (AH) and diabetes. Numerous studies have revealed the presence of various pathological changes in the brain, in particular foci of gliosis and leukoaraiosis, and have established a link between the formation of foci of leukoaraiosis and development of CD in these patients [Starchina UA, 2006; Evstigneev VV, 2009; Levin OS, 2011].

AF is one of the important risk factors for the development of vascular pathology of the brain. Characteristic for patients with AF is increased risk of getting ischemic stroke and widespread chronic disorders of brain circulation. Reduction of cardiac output and the contractile function of the heart cause impaired cerebral blood flow, contributing to the formation and/or progression of CD (memory decline, deficit of attention, intellectual impairment and slowing of mental processes), which subsequently can reach the degree of dementia [Yahno NN, 2006; Lane DA et al., 2009; Puccio D et al., 2009]. Recent studies provide data on reliable connection between AF and the risk of vascular dementia [Almeida OP, Flicker L, 2001; Yahno NN et al., 2005; Woo MA et al., 2009; Alekhine AN et al., 2011].

The problem of dementia in modern medicine is becoming one of the most urgent ones, which is associated with a marked deterioration in the quality of life for patients suffering from this disease and consequent disability. Huge socio-economic losses incurred by society are associated with the development of cognitive deficits.

The search and study of links between the brain condition and cognitive dysfunction in patients with AF seem important and rather interesting. White matter in the deep regions of hemispheres is one of the most hypoperfusion-sensitive areas of the brain [Jelic V et al., 2006; Levin OS, 2011]. This is accounted for by several factors. White matter is supplied with blood via long thin penetrating arteries that branch away at right angles from the surface of large vessels and almost have no collaterals. In addition, regional blood flow in white matter is about 1/4 of the volume of the blood flow in grey matter; in the presence of mod-

erate but prolonged hypotension when the blood flow in both zones is reduced by one and the same absolute value, it gets below the critical level in white matter and above it in the grey matter, which provides further possibility for fuller recovery [Sushlina ZA et al., 2010; Levin OS, 2011].

Since AF poses a high risk of developing micro- and macrovascular complications, study of the early manifestations of cerebrovascular insufficiency in this group of patients is of particular importance.

Despite intensive studies of the role of AF in the development of CD, this problem still raises a lot of questions. Understudied is the role of CD as symptoms of brain lesions in patients with AF. In the Ukrainian literature there are no comprehensive studies on the qualitative and quantitative neuropsychological analysis of the CD semiotics, not reaching the degree of dementia in the presence of AF. There is no common opinion about the factors affecting the development of cognitive dysfunction in AF.

The objective of this study was to examine manifestations of chronic cerebrovascular pathology in patients with different clinical forms of AF based on clinical, neurological and neuropsychological research.

#### MATERIALS AND METHODS

Eighty two patients were examined with different clinical forms of AF aged 45 to 70 years (mean age of  $62.4 \pm 5.6$  years), among them 68 men and 14 women (study group) and 30 patients aged 50 to 70 years (average of  $62.3 \pm 4.8$  years) without any cardiac rhythm and conduction, including 22 men, 8 women (comparison group). Forty four (53.7%) patients had permanent AF and 38 (46.3%) had persistent or paroxysmal AF. The groups were matched for age and gender.

Excluded from the study were patients with previous stroke, end-stage somatic diseases, multiple organ failure, inflammatory and traumatic lesions and neoplasms of the central nervous system, mental illness, which ruled out the possibility to assess cognitive functions, severe emotional and behavioral disorders (depression, anxiety).

All patients were given a comprehensive clinical-neurological, neuropsychological, laboratory and instrumental examination at the the cardiology

clinic of the Military Medical Clinical Center of the Western Region, Lviv). The study was conducted in accordance with the WMA Declaration of Helsinki. The research protocol was approved by the clinical center's research ethics committee.

Clinical-neurological study included structured collection of complaints, medical history information, examination, and testing of the neurological state.

Neuropsychological study included testing using a range of scales and tests. As there is currently no universally accepted set of neuropsychological tests for the diagnosis of mild cognitive dysfunction, there were selected formalized screening methods with quantitative evaluation of the obtained results allowing for assessing basic cognitive functions (memory, attention, language, visual-spatial function and regulation of any activity). The following methods were used in the study: the Global Deterioration Scale of cognitive functions (GDS), the Mini-Mental State Examination (MMSE), the Frontal Assessment Battery (FAB), the clock drawing test, and the Controlled Oral Word Association Test (COWAT). In-depth study of cognitive functions in patients under examination also included more detailed tests, which, in addition to the quantitative evaluation, allowed for conducting a qualitative analysis to identify deviations (tests on memorizing 10 words), the Grober and Buske 12-words test, and the Schulte sample. Before conducting neuropsychological testing, all patients were offered a questionnaire to assess the presence and severity of depressive symptoms (Beck depression scale) and evaluation of the level of situational (reactive) anxiety (Spielberger-Hanina test) [Bleisher VM et al., 2002].

Instrumental examination of the study included daily monitoring of blood pressure, heart rate, ECG, and brain CT. Daily monitoring with determination of mean values of systolic blood pressure (SBP) and diastolic blood pressure (DBP), heart rate was carried out on the InnoCare-5 monitoring system (Hungary). Localization, the nature and severity of focal and diffuse changes in the brain were examined by CT scanner Asteion 4 mod. TSX-021B (Japan). A qualitative assessment of the CT results included the identification of focal and diffuse changes of the brain. Quantitative assessment of the changes was carried out using a num-

ber of methods for point system: determination of the intensity changes of the white matter in the periventricular [Liu CK, Miller BI, 1992] and subcortical regions [Fazekas F et al., 1987; Yahno NN et al., 2001], and the severity of enlarged perivascular spaces (EPS) [MacLulich AMJ et al., 2004].

Statistical processing of the obtained results was performed using SPSS 13.0. Descriptive statistics for normal distribution of the trait (in accordance with the results of the Kolmogorov-Smirnov test) were presented as mean values and standard deviations ( $M \pm SD$ ). Descriptive statistics was presented in median (Me) values and 25 and 75 percentile values (interquartile scale) in the distribution of a trait different from normal one. Minimum and maximum values (Maximum, Minimum) were additionally used for some indices. Descriptive statistics of qualitative traits were also presented as absolute and relative frequencies (percentages). For comparison of two independent groups based on one variable were used Whitney-Mann U-test,  $\chi^2$  test and Fisher's exact test (in cases of small samples). Comparison of two dependent groups based on one variable was conducted using Wilcoxon and McNemar criterion (in the presence of dichotomous variables). Comparison of three independent groups on one-by-one basis was run using a one-way ANOVA variation in Kruskal-Wallis test. Statistically significant differences were considered with  $p < 0.05$ . Spearman nonparametric correlation analysis was used for determining the relationship between two attributes. To rule out distorting variables calculation of special correlation was performed.

## RESULTS AND DISCUSSION

Patients with AF had more burdened vascular disease (hypertension, ischemic heart disease) compared with patients without AF. 90.2% of AF patients were diagnosed with hypertension, 85.4% with ischemic heart disease, or 15.9% of patients suffered a myocardial infarction. Patients in both groups significantly differed in the values of body mass index (BMI), cholesterol and triglycerides (Table 1).

For the analysis of neurological and neuropsychological features of brain lesions in the presence of AF all patients of the main group were divided into two subgroups: with persistent or paroxysmal AF form (subgroup 1) and with the permanent AF

Table 1.

## Clinical and laboratory characteristics of patients of the main group and comparison group

Characteristics	Groups	
	Main (n=82)	Comparison (n=30)
Presence of arterial hypertension	74 (90.2%)	16 (53.3%)**
Duration of arterial hypertension, years	15 (8;25)	12 (5;22)
Average systolic blood pressure, mmHg	152.4±16.2	136.2±12.6**
Average diastolic blood pressure, mmHg	86.6±10.2	75.6±6.4**
Average heart rate	98.2±8.2	78.4±6.4**
Body mass index, kg/m <sup>2</sup>	31 (28;34)	26 (22;28)**
Cholesterol, mmol/l	6.2±1.8	5.8±1.0
Triglycerides, mmol/l	2.2±1.4	1.4±0.4*
Low-density lipoprotein, mmol/l	4.4±0.8	3.8±0.6
High-density lipoprotein, mmol/l	1.3±0.4	1.6±0.5

Notes: \*\* - differences at the significance level of  $p < 0.001$ ;

\* - differences at the significance level of  $p < 0.05$

TABLE 2.

## The main clinical and laboratory characteristics of patients with atrial fibrillation

Characteristics	Subgroup 1 (n=38)	Subgroup 2 (n=44)
Mean age, years	60.8±5.2	64.2±5.8
Age, years	45-70	48-70
Men / Women	32 (84.2%) / 6 (15.8%)	36 (81.8%)/8 (18.2%)
Duration of arterial hypertension, years	12.2±5.8	18.4±6.6*
Average systolic blood pressure, mmHg	146.6±12.4	155.2±16.4
Average diastolic blood pressure mmHg	79.6±8.1	89.1±8.3
Average heart rate bpm	92.2±7.8	100.6±6.8
Body mass index, kg/m <sup>2</sup>	30 (27; 35)	31 (28; 33)
Cholesterol, mmol/l	6.0±1.2	6.3±1.6
Triglycerides, mmol/l	2.1±1.5	2.3±1.6
Ischemic heart disease	26 (68.4%)	44 (100.0%)**
Myocardial infarction in medical history	4 (10.5%)	9 (20.5%)*
Low-density lipoprotein, mmol/l	4.3±0.7	4.5±0.8
High-density lipoprotein, mmol/l	1.4±0.4	1.3±0.3

Notes: \*\* - differences at the significance level of  $p < 0.001$ ;

\* - differences at the significance level of  $p < 0.05$

form (subgroup 2). Both groups were matched for age, gender and the number of patients with hypertension. Patients with permanent forms of AF exhibited higher levels of DBP - they more often had a history of ischemic heart disease (Table 2).

Patients in both groups complained of memory impairment. Closer inquiry revealed that by memory impairment the patients understood precisely forgetfulness, confusion, word-finding difficulty, fatigue, and decreased performance. Patients also complained of headache, vertigo of non-systemic nature, and noise in the head (Table 3).

Examination of the neurological state of the patients in both groups revealed minimum focal neurological symptoms as symptoms of oral automatism and vestibular-ataxic disorders (instability in

the Romberg stance, inaccuracy when performing coordination tests).

Patients with permanent form of AF frequently complained of absent-mindedness (Fisher's exact test,  $p=0.042$ ), word-finding difficulty when speaking (Fisher's exact test,  $p=0.025$ ). Patients with permanent AF form also exhibited more pronounced minimum focal neurological symptoms in the form of vestibular-ataxic disorders than in patients with persistent (paroxysmal) AF form (Fisher's exact test,  $p=0.024$ ).

Before neuropsychological testing, patients in both groups performed tests of the presence and severity of depressive symptoms (Beck's depression scale) and assessment of the level of situational (reactive) anxiety (RA) (Spielberger-Hanina test) to rule

TABLE 3.

## Complaints and focal neurological symptoms in patients

Clinical characteristics of the groups	Subgroup 1 (n=38)	Subgroup 2 (n=44)	The comparison group (n=30)
Headache	6 (15.8%)	14 (31.8%)	5 (16.7%)**
Vertigo non-systemic nature	8 (21.1%)	16 (36.4%)	6 (20.0%)
Noise in the head	4 (10.5%)	5 (11.4%)	2 (6.7%)
Memory impairment	17 (44.7%)	30 (68.2%)	10 (33.3%)*
Fatigue, decreased performance	10 (26.3%)	13 (29.5%)	15 (50.0%)*
Word-finding difficulty	13 (34.2%)	29 (65.9%)*	5 (16.7%)*
Confusion	15 (39.5%)	28 (63.6%)*	11 (36.7%)
The symptoms of oral automatism	9 (23.7%)	19 (43.2%)	6 (20.0%)
Vestibular-ataxic disorders	14 (36.8%)	30 (68.2%)*	9 (30.0%)

Notes: \*\* - differences at the significance level of  $p<0.001$ ;

\* - differences at the significance level of  $p<0.05$

TABLE 4.

## The level of depression and anxiety in patients studied

Name of the test	Interpretation of the test	Subgroup 1 (n=38)	Subgroup 2 (n=44)	The comparison group (n=30)
Beck's Depression Scale	0 - 9 points (no depression)	18 (47.4%)	15 (34.1%)	19 (63.3%)
	10 - 15 points (minor depressive disorder)	20 (52.6%)	29 (65.9%)	11 (36.7%)
Spielberger-Hanina Test (for reactive anxiety)	Low	7 (18.4%)	5 (11.4%)	6 (20.0%)
	Moderate	21 (55.3%)	25 (56.8%)	18 (60.0%)
	High	10 (26.3%)	14 (31.8%)	6 (20.0%)

out "dysthymic" type of CD. Express depressive disorders were not identified. Most patients showed a moderate level of situational anxiety (table 4).

The test results based on the General Deterioration Scale (GDS) showed that patients did not exhibit significant cognitive deficits, however, and patients with permanent forms of AF in many cases corresponded to GDS stage 3 than patients with persistent (paroxysmal) form of AF. There were also no significant deviations of cognitive functions in patients of different groups according to MMSE and Battery of frontal dysfunction test results.

Statistically significant differences between the groups were obtained by performing a Controlled Oral Word Association Test, clock drawing test, and using Schulte table. It was found that patients with AF named fewer words with the letter 'S' per minute in general than the patients in the comparison group. Those with permanent form of AF performed worse on the clock drawing test and slower on Schulte test.

AF patients also exhibited memory impairment. During the 10-words memorization test the AF patients more frequently exhibited light and moderate memory impairment and attention deficit than the patients in the comparison group. The patients with permanent AF showed increase in the intensity of memory disorders and no significant increase in attention deficit.

The Grober and Buske test (12-words memorization test using semantic prompts; immediate and delayed reproduction, with and without a prompt) has allowed for dividing memory impairment in the patients of both groups into amnesic and non-amnesic. The results of this test revealed that memory impairment was observed more frequently in patients with AF – in a larger percentage of cases they were of non-amnesic nature.

Neuropsychological study of patients with AF and those without AF, matched for age and gender, showed that the AF patients performed reliably worse on the Schulte test and Controlled Oral Word Association Test. It revealed apparent presence of impaired attention, mental pace, and fluency of speech. AF patients more often exhibit disorders of visual-spatial functions (clock drawing test results) and memory impairment compared to patients without AF. The latter in most cases are of secondary nature, resulting from deficit of atten-

tion. The changes identified correspond to light neurodynamics CD.

Neurodynamics disorders are increasing in the presence of permanent AF, mainly due to deceleration of mental processes, whereas attention deficit and reduction in the speech rate is changing slightly. In addition, permanent AF form accounts for enhanced visual-spatial disorders and mental disorders.

The results of neuropsychological tests in patients of different groups are shown in table 5.

In patients of both groups CT scan revealed a lesion of the brain's white matter in the form of leukoaraiosis (subcortical and periventricular) and expansion of periventricular spaces. "Silent" infarctions were detected in 24 patients of the main group.

Diffuse changes in the brain's white matter were more prevalent in patients with AF. Differences in the detection rate of leukoaraiosis and that of the EPS between the two groups were statistically significant. Patients with permanent AF form exhibited more changes in white matter in the periventricular areas (Fig. 1).

Patient groups were compared by rating scale medians of periventricular, subcortical leukoaraiosis and enlarged periventricular spaces. The severity of the changes of the brain's white matter was different in the study and comparison groups. The severity of periventricular leukoaraiosis in some patients of the main group reached the first degree, which corresponded to limited changes of the periventricular white matter in front or rear regions. Several studies consider such changes a variant of the age norm [Fazekas F et al., 1993; Schmidt R et al., 2002]. At the same time, the changes in the

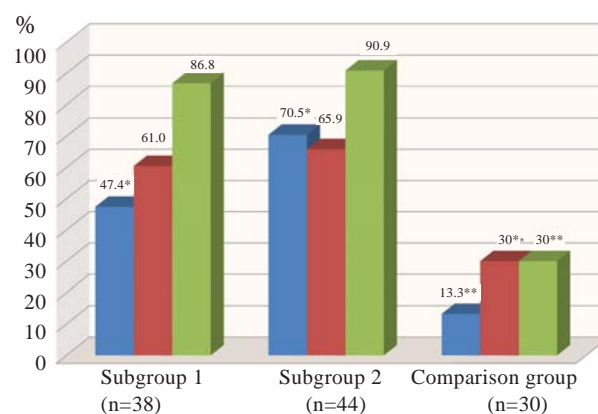


FIGURE 1. Changes in the brain CT scan of patients.

NOTE: ■ periventricular leukoaraiosis, ■ subcortical leukoaraiosis, ■ enlarged perivascular spaces.

TABLE 5.

## The results of neuropsychological testing of patients

Name of the test	Interpretation of the test	Subgroup 1 (n=38)	Subgroup 2 (n=44)	Comparison group (n=30)
Global Deterioration Scale	Points corresponding to the severity of cognitive deficits	1.7±0.6	2.0±0.4**	1.8±0.6
Mini-Mental State Examination	Average point	27.8±1.0	27.4±1.2	28.0±0.8
Frontal Assessment Battery	Average point	16.1±0.6	15.8±1.1	16.3±0.9
Controlled Oral Word Association Test	Number of patients who named less than 10 words per minute	10 (26.3%)	15 (34.1%)	4 (13.3%)*
	Number of patients who named more than 10 words per minute	28 (73.7%)	29 (65.9%)	26 (86.7%)*
Clock drawing test (points)	Average point	8.0±1.4	7.6±1.6*	8.4±1.6*
Schulte test (seconds)	Average time of test	46.1±8.8	50.1±10.4*	43.2±7.2*
	Memory impairment is not identified (9/10 words by the third reproduction)	10 (26.3%)	6 (13.6%)*	11 (36.7%)**
	Light memory impairment (8/7 words by the third reproduction)	20 (52.6%)	19 (43.2%)*	13 (43.3%)**
	Moderate memory impairment (5/6 words by the third reproduction)	8 (21.1%)	17 (38.6%)*	6 (20.0%)**
	Acute memory impairment (3/4 of words by the third reproduction)	0	2 (4.6%)*	0**
	Distraction	25 (65.8%)	30 (68.2%)	13 (43.3%)*
	Impairment not identified	13 (34.2%)	14 (31.8%)	17 (56.7%)*
	No memory disorders	11 (28.9%)**	8 (18.1%)	11 (36.7%)
Grober and Buske Test	Neumaticos disorders	24 (63.2%)**	31 (70.5%)	17 (56.7%)
	Amnesic disorders	3 (7.9%)**	5 (11.4%)	2 (6.7%)

Notes: \*\* - differences at the significance level of  $p < 0.001$ ;

\* - differences at the significance level of  $p < 0.05$

periventricular white matter in the comparison group did not reach such severity as in the group of AF patients. The severity of periventricular leukoaraiosis in the main group was statistically more significant than in the comparison group.

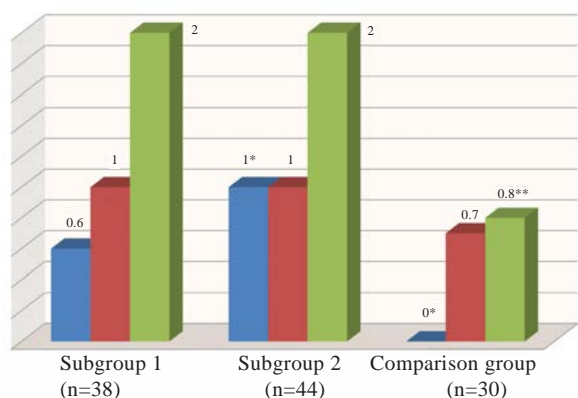
Changes in the brain's white matter in the form of subcortical leukoaraiosis were not pronounced. In most patients of the main group and the comparison group less than 5 small local lesions 5 mm in diameter or less than 2 large local lesions in 5-10 mm diameter were detected. The differences between both groups in the number and size of de-

tected lesions in subcortical white matter were not statistically significant.

Both groups' differences in severity of the EPS were most significant.

In particular, scans of the AF patient group most frequently revealed 10 to 20 hyperintense lesions 1-2 mm in diameter in locations of perforating arteries perpendicular to the brain surface. In the comparison group most frequently less than 10 of such lesions were detected.

In patients with permanent AF form periventricular leukoaraiosis was more severe. Statisti-



**FIGURE 2.** The severity (in points) changes in brain CT scan in patients studied.

**NOTE:** ■ periventricular leukoaraiosis, ■ subcortical leukoaraiosis, ■ enlarged perivascular spaces.

cally significant differences in the severity of subcortical leukoaraiosis and enlarged periventricular spaces in patients with different forms of AF were not obtained (Fig. 2).

Spearman correlation analysis revealed moderate direct correlation between the severity of periventricular leukoaraiosis and impaired memory according to 10-words memorization test results (Spearman test,  $r=0.248$ ,  $p=0.008$ ,  $N=119$ ) and Schulte test runtime (Spearman test,  $r=0.287$ ,  $p=0.004$ ,  $N=123$ ), as well as a direct statistically significant relationship between the severity of subcortical leukoaraiosis and memory disorders (Spearman test,  $r=0.265$ ,  $p=0.006$ ,  $N=118$ ).

Based on the results of the Spearman correlation analysis it was found that progressive changes in the cerebral white matter is clinically linked to the development of cognitive dysfunction expressed in deterioration of memory, attention and mental speed. The study made it possible to clarify the factors of brain lesion pathogenesis in AF. The progression of periventricular leukoaraiosis depends mainly on the presence and compensation of AG. Moderate direct correlation was found between the severity of periventricular leukoaraiosis and the duration of hypertension (Spearman test,  $r=0.387$ ,  $p<0.001$ ,  $N=121$ ) and average SBP (Spearman test,  $r=0.384$ ,  $p<0.001$ ,  $N=121$ ), aver-

age DBP (Spearman test,  $r=0.198$ ,  $p=0.035$ ,  $N=121$ ). Mainly age, not AG, exerts effect on the development of subcortical leukoaraiosis (Spearman test,  $r=0.287$ ,  $p=0.001$ ,  $N=125$ ). Vascular factors (AH) play the role in the pathogenesis of progression of perivascular space expansion in AF (Spearman test,  $r=0.355$ ,  $p<0.001$ ,  $N=121$ ).

## CONCLUSION

Early manifestations of chronic disorders of cerebral circulation in patients with atrial fibrillation in the absence of severe focal neurological symptoms may be mild cognitive disorders, the identification of which is necessary due to the increased risk of progression to the stage of severe cognitive deficits.

Cognitive disorders in patients with AF without stroke history are attention deficit, reduced rate of speech and mental activity, impaired visual-spatial functions and secondary memory disorders. These disorders fall within the light cognitive disorders of the neurodynamics nature. The permanent AF form is linked to progressive reduction in the psychomotor speed, visual-spatial disorders and reduction of memory, whereas deterioration of cognitive functions occurs regardless of age, duration of hypertension and indicators of dyslipidemia disorders.

The presence of AF is associated with a higher incidence of diffuse lesions of the brain's white matter. The most pronounced changes in the brain in patients with AF are detected in the periventricular matter and perivascular spaces. In the presence of permanent form of AF progressive changes occur in the periventricular white matter of the brain. AH plays the most significant role in the progression of periventricular leukoaraiosis in permanent AF. The severity of subcortical leukoaraiosis and perivascular space expansion in permanent form of AF progresses slightly. Progression of subcortical leukoaraiosis is associated mainly with aging. Vascular factors (hypertension) play the role in the pathogenesis of progression of perivascular space expansion in AF. Progression of diffuse changes in the brain's white matter is associated with the development of disorders of memory, attention and mental speed.

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