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ABSTRACT

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PREDICTORS OF COGNITIVE DETERIORATION DURING THE FIRST YEAR AFTER ISCHEMIC NON-LACUNAR STROKES IN PATIENTS WITH ATRIAL FIBRILLATION

Introduction. Epidemiological studies revealed that AF may be an independent predictor of cognitive impairment, including post-stroke patients. AF patients had statistically significant deterioration of cognitive functioning during the first year after ischemic strokes. However, the factors associated with cognitive deterioration during the post-stroke period in AF patients have not yet been identified.

Objective: to study the factors associated with cognitive deterioration during the first year after ischemic non-lacunar strokes in patients with AF.

Materials. In the final analysis, we included 65 patients with AF who had an ischemic non-lacunar stroke within the last 6 months. The cognitive assessment consisted of a Mini-Mental State Examination, Montreal Cognitive Assessment, Clock Drawing Test, and Frontal Assessment Battery. "Cognitive deterioration" was defined as ≥ 1 point decrease by any of the cognitive scales at the 12-month visit compared to the initial visit score. As predictors of cognitive deterioration, we studied socio-demographic, psycho-emotional, comorbid, neurological, functional, neuroimaging factors, lipid profile, and transthoracic echocardiographic parameters.

Results. According to all of the used cognitive scales, the same factors were independent predictors of cognitive deterioration during the first year after ischemic non-lacunar strokes in patients with AF – severe leukoaraiosis (Fazekas scale score >3), reduced left ventricle ejection fraction and increased left atrium size. The optimal thresholds of left ventricle ejection fraction values for predicting cognitive deterioration, depending on the cognitive scale, were within the interval of 41–48%, whereas the optimal threshold of left atrium size for predicting cognitive deterioration, regardless of the scale used, was the same – 41 mm.

Conclusions. Independent predictors of cognitive deterioration in AF patients during the first year after ischemic non-lacunar strokes are leukoaraiosis, low left ventricle ejection fraction, and high left atrium size.

Keywords: ischemic stroke, atrial fibrillation, cognitive impairment, predictors, leukoaraiosis, echocardiography.

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ПРЕДИКТОРИ ПОГІРШЕННЯ КОГНІТИВНИХ ФУНКЦІЙ ПРОТЯГОМ ПЕРШОГО РОКУ ПІСЛЯ ІШЕМІЧНОГО НЕЛАКУНАРНОГО ІНСУЛЬТУ У ПАЦІЄНТІВ З ФІБРИЛЯЦІЄЮ ПЕРЕДСЕРДЬ

Вступ. Епідеміологічні дослідження виявили, що ФП є незалежним предиктором когнітивних порушень, у тому числі у пацієнтів з інсультами. Проспективно показано, що пацієнти з ФП мають значуще погіршення когнітивних функцій протягом першого року після ішемічного інсульту. Однак до теперішнього часу не визначені фактори, пов'язані з негативною когнітивною динамікою після інсульту у пацієнтів з ФП.

Мета: вивчити предиктори погіршення когнітивних функцій протягом першого року після ішемічного нелакунарного інсульту у пацієнтів з ФП.

Матеріали. В остаточний аналіз включено 65 пацієнтів з ФП, які перенесли ішемічний нелакунарний інсульт протягом останніх 6 місяців. Когнітивна оцінка складалася з короткої шкали оцінки психічного статусу, Монреальської шкали оцінки когнітивних функцій, тесту малювання годинника та батареї лобної дисфункції. «Когнітивне погіршення» визначалося як зниження показників будь-якої з когнітивних шкал на 1 бал та більше під час 12-місячного візиту, порівняно з початковим обстеженням. В якості можливих предикторів когнітивного погіршення вивчалися соціально-демографічні, психоемоційні, коморбідні, неврологічні, функціональні, нейровізуалізаційні фактори, ліпідограма та параметри трансторакальної ехокардіографії.

Результати. Погіршення когнітивних функцій згідно усіх використаних когнітивних шкал у пацієнтів з ФП протягом першого року після ішемічного нелакунарного інсульту незалежно асоціювалося з ідентичними фактори – з «вираженим» лейкоареозом (за шкалою Фазекас > 3 балів), зі зниженою фракцією викиду лівого шлуночка та зі збільшеними розмірами лівого передсердя. Порогові значення фракції викиду лівого шлуночка, що асоціюються з когнітивним погіршенням, залежно від шкали коливалися, і знаходилися в інтервалі 41–48%; поріг розміру лівого передсердя, що асоціювався з когнітивним погіршенням, незалежно від використаної шкали, був однаковим і становив 41 мм.

Висновки. Незалежними предикторами погіршення когнітивних функцій у пацієнтів з ФП протягом першого року після ішемічного нелакунарного інсульту є виражений лейкоареоз, знижена фракція викиду лівого шлуночка та збільшені розміри лівого передсердя.

Ключові слова: ішемічний інсульт, фібриляція передсердь, когнітивні порушення, предиктори, лейкоареоз, ехокардіографія.

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ABBREVIATIONS

AF – atrial fibrillation
AUC – area under the curve
CDT – Clock Drawing Test
CD – cognitive decline
CI – confidence interval
FAB – Frontal Assessment Battery
HDL – high density lipoproteins
LAS – left atrium size
LDL – low density lipoprotein
LVEDD – left ventricular end-diastolic diameter
LVEDV – left ventricular end-diastolic volume
LVEF – left ventricle ejection fraction
LVESD – left ventricular end-systolic diameter
LVESV – left ventricular end-systolic volume
Me – median
MMSE – Mini Mental State Examination
MoCA – Montreal Cognitive Assessment
MRS – modified Rankin scale
NIHSS – National Institute of Health Stroke Scale
OR – odds ratio
Q1–Q3 – interquartile range
ROC – receiver operating characteristics
TCH – total cholesterol
TG – triglycerides

INTRODUCTION

In recent years, a new trend in clinical neurology is the intensive study of cognitive, psycho-emotional, and neuropsychological aspects of nervous system diseases [1, 2, 3]. This issue is particularly critical in the context of the medical and social consequences of the current Russia-Ukraine war [4, 5].

Atrial fibrillation (AF) and cognitive decline (CD) are serious public health issues that place a heavy strain on medical resources [6]. Previous epidemiological studies suggested that AF may be an independent predictor of CD, regardless of the presence of common risk factors including age, diabetes, hypertension, heart failure, etc. [7, 8].

On the other hand, the risk of stroke is increased as much as five-fold in patients with AF, which in turn can increase the risk of post-stroke CD and dementia [9]. For example, in the general population, 10% of patients develop dementia after a first stroke [10]. In people with a history of stroke, AF may be associated with a higher risk of dementia or CD [11]. Moreover, it was found that AF is a significant risk factor for post-stroke CD, even after correcting for AF-related infarcts [12].

The cognitive condition of stroke survivors has been viewed in recent decades as a dynamic phenomenon with variable trends, particularly within the first year following the beginning of the stroke [13]. In particular, we have demonstrated that, in comparison to patients with normal sinus rhythm, those with permanent (paroxysmal) and persistent AF had statistically significant negative changes in cognitive functioning during the first year after ischemic non-lacunar strokes [14].

To date, the factors associated with CD after stroke in AF patients have not been clearly identified. However, knowledge of these factors can be the basis for early prevention or delay of the occurrence and progression of cognitive impairment.

Objective: to study the factors associated with cognitive deterioration during the first year after ischemic non-lacunar strokes in patients with AF.

MATERIAL AND METHODS. This study was approved by the Ethics Committee of Poltava State Medical University, in accordance with the Declaration of Helsinki (protocol №189/2020). The written informed consent was obtained for all patients before their inclusion in the study.

Criteria for inclusion of patients in the study.

1. Ischemic non-lacunar stroke occurring within the last 6 months.
2. AF due to ischemic heart disease and (or) arterial hypertension.
3. Age from 18 to 75 years.
4. Written patient consent.

Criteria for exclusion of patients from the study.

1. Documented cognitive impairment in the pre-stroke period.
2. Speech disorders that significantly limit communication with the patient.
3. Impaired writing function, which does not allow for proper completion of the questionnaires.
4. Concomitant neurological diseases that can cause cognitive disorders/
5. Decompensated somatic pathology.
6. Psychiatric and narcological pathology.
7. Use of psychoactive drugs that affect cognitive functions.

We recruited 63 patients with a persistent or paroxysmal form of AF (53 patients within 3 months and 10 patients within 3–6 months after stroke occurrence) and 40 patients with a permanent form of

AF (32 patients within 3 months and 8 patients within 3–6 months after stroke occurrence).

All included patients underwent an assessment of cognitive functions after the inclusion in the study and then at 12 months following the stroke. We used several cognitive scales – Mini Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA), Clock Drawing Test (CDT), and Frontal Assessment Battery (FAB). “Cognitive deterioration” was defined as the state of decreasing the value of any used cognitive scale by 1 point or more at the 12-month visit compared to the initial value.

We recorded the following socio-demographic data: age, gender, level of education (higher / non-higher), marital status (married / single), current employment, and "smokers’ status" (those who smoked regularly during the last year).

Anxiety and depression were diagnosed by using the Hospital Anxiety and Depression Scale by values of the anxiety and depression subscales ≥11. Fatigue was assessed by using the Fatigue Severity Scale with a critical value of ≥4 points.

We considered comorbidities that had a prevalence rate of at least 5% in the sample, including abdominal obesity (waist circumference ≥ 102 cm for men and ≥88 cm for women), arterial hypertension, diabetes mellitus and peripheral artery disease.

The neurological and functional outcomes were assessed by National Institute of Health Stroke Scale (NIHSS) and modified Rankin scale (MRS). The characteristics of stroke included the affected cerebral hemisphere and primary-secondary stroke nature.

Neuroimaging characteristics included stroke localization (supratentorial / infratentorial), cerebral infarct volume using the ellipsoid formula, and leukoaraiosis prevalence using the Fazekas scale.

We also analyzed the blood lipid profile: total cholesterol (TCH), high density lipoproteins (HDL), low density lipoprotein (LDL) and triglycerides (TG).

All patients underwent transthoracic echocardiography with assessment the following echocardiographic parameters: left ventricular end-diastolic diameter (LVEDD), left ventricular end-systolic diameter (LVESD), left ventricular end-diastolic volume (LVEDV), left ventricular end-systolic volume (LVESV), left ventricle ejection fraction (LVEF), left atrium size (LAS).

Quantitative values were presented as median (Me) and interquartile range (Q1–Q3). Qualitative values were presented as numbers and percentages. Quantitative values were compared using the nonparametric Mann–Whitney U-test. Qualitative variables were compared using Fisher's exact test. Univariate logistic regression analysis was performed to analyze the odds ratio (OR) with 95% confidence interval (CI) of factors associated with cognitive deterioration. Variables having a p-value less than 0.05 in the univariate analysis were selected and evaluated by multivariate logistic regression models. To assess the diagnostic value of quantitative characteristics in predicting cognitive deterioration, the method of receiver operating characteristics (ROC) curve analysis was used with calculation of the area under the curve (AUC), sensitivity, and specificity of the model with a 95% CI. The optimal threshold value in ROC analysis was determined by the highest value of the Youden index. Differences at $p < 0.05$ were considered significant.

RESULTS

During the follow-up, patients dropped out of the study for various reasons, including death, relocation, transportation issues, and an unwillingness to continue cooperating. In the persistent (paroxysmal) AF group, 23 patients dropped out of the study (dropout rate 36.5%). The dropout rate in the permanent AF group was 15 (37.5%). Thus, in the final analysis, 65 patients were included.

Table 1 shows patients’ characteristics at the initial visit.

Patients took oral anticoagulants (direct – 46 (70.8%), indirect – 15 (23.1%)), antihypertensive drugs (62 (95.4%)), statins (59 (90.8%)), and antiarrhythmics (34 (52.3%)).

During observation period cognitive deterioration was documented in 38 (57%) patients according to MMSE, in 41 (63.1%) according to MoCA, in 40 (61.6%) according to CDT, and in 41 patients (63.1%) according to FAB.

First of all, it should be noted that gender, level of education, employment status, marital status, smoking status, abdominal obesity, arterial hypertension, ischemic heart disease, diabetes mellitus, peripheral artery disease, NIHSS score, MRS score, depression, anxiety, fatigue, primary stroke nature, TCH, HDL, LDL, TG, infarct volume, affected cerebral hemisphere, supratentorial / infratentorial stroke localization, LVEDD, LVESD, LVEDV, LVESV had no significant associations with cognitive deterioration on any of the cognitive scales during the observation period.

Due to the limitations of the paper, we present only statistically significant differences between patients with cognitive deterioration and patients without cognitive deterioration (who had cognitive stability and cognitive improvement) according to each of the used scales.

Table 1 – Baseline characteristics of study participants

Factor		Value
age (years), Me (Q1-Q3)		70.0 (65.0-72.0)
male gender, n (%)		39 (60.0%)
higher education, n (%)		17 (26.2%)
employment, n (%)		7 (10.8%)
married, n (%)		42 (64.6%)
smoker, n (%)		5 (7.7%)
chronic heart failure, stage	I	29 (44.6%)
	IIA	34 (52.3%)
	IIB	2 (3.1%)
abdominal obesity, n (%)		19 (29.2%)
arterial hypertension, n (%)		60 (92.3%)
ischemic heart disease n (%)		58 (89.2%)
diabetes mellitus, n (%)		13 (29.2%)
peripheral artery disease, n (%)		10 (15.4%)
NIHSS (points), Me (Q1-Q3)		11.0 (9.0-13.0)
MRS (points)	≤ 2, n (%)	22 (33.8%)
	> 2, n (%)	43 (66.2%)
secondary stroke, n (%)		8 (12.3%)
depression, n (%)		21 (32.3%)
anxiety, n (%)		22 (33.8%)
fatigue, n (%)		33 (50.8%)
TCH (mmol/l), Me (Q1-Q3)		5.31 (4.35-6.07)
HDL (mmol/l), Me (Q1-Q3)		1.26 (1.08-1.53)
LDL (mmol/l), Me (Q1-Q3)		3.01 (2.50-3.56)
TG (mmol/l), Me (Q1-Q3)		1.27 (0.96-1.79)
Stroke volume (cm^3), Me (Q1-Q3)		15.0 (10.0-26.0)
Fazekas scale (points)	<3, n (%)	43 (66.2%)
	>3, n (%)	22 (33.8%)
supratentorial stroke, n (%)		53 (81.5%)
affected cerebral hemisphere	Right, n (%)	34 (52.3%)
	Left, n (%)	31 (47.7%)
LVEDD (mm), Me (Q1-Q3)		50.0 (48.0-56.0)
LVESD (mm), Me (Q1-Q3)		37.0 (35.0-43.0)
LVEDV (ml), Me (Q1-Q3)		124.0 (108.0-156.0)
LVESV (ml), Me (Q1-Q3)		56.0 (48.0-65.0)
LVEF (%), Me (Q1-Q3)		47.0 (41.0-54.0)
LAS (mm), Me (Q1-Q3)		42.0 (40.0-45.0)

Table 2 – Factors associated with cognitive deterioration according to MMSE

Factor		Cognitive outcome		P
		deterioration	non-deterioration	
age (years), Me (Q1-Q3)		71.0 (69.0-73.0)	67.0 (63.5-70.5)	$p_1 = 0.02$
Fazekas scale (points)	<3, n (%)	21 (55.3%)	22 (81.5%)	$p_2 = 0.04$
	>3, n (%)	17 (44.7%)	5 (18.5%)	
LVEF (%), Me (Q1-Q3)		43.0 (38.0-48.0)	51.0 (47.5-54.0)	$p_1<0.01$
LAS (mm), Me (Q1-Q3)		44.5 (42.0-48.0)	40.0 (38.0-42.0)	$p_1<0.01$

Note:
p_1 – a statistically significant difference, according to the Mann–Whitney U test;
p_2 – a statistically significant difference, according to the Fisher exact test

Table 2 demonstrates that patients with cognitive deterioration due to MMSE had statistically older age, higher proportion of severe leukoaraiosis, lower LVEF, and higher LAS. In the univariate logistic regression analysis, as predictors for cognitive deterioration were an increase in patients' age (OR 1.12; 95% CI, 1.01–1.23; p = 0.03), Fazekas scale score > 3 points (OR 3.56; 95% CI, 1.11–11.39; p = 0.03), reduced LVEF (OR 0.85; 95% CI, 0.77–0.93; p<0.01), and increased LAS (OR 1.27; 95% CI, 1.09–1.47; p<0.01). The multivariate logistic regression analysis revealed that independent predictors for cognitive deterioration were Fazekas scale score > 3 points (OR 5.28; 95% CI, 1.12–24.91; p = 0.04), reduced LVEF (OR 0.89; 95% CI, 0.80–0.99; p = 0.03) and increased LAS (OR 1.25; 95% CI, 1.04–1.51; p = 0.02).

Table 3 – Factors associated with cognitive deterioration according to MoCA

Factor		Cognitive outcome		P
		deterioration	non-deterioration	
Fazekas scale (points)	<3, n (%)	22 (53.7%)	21 (87.5%)	$p_2 = 0.01$
	>3, n (%)	19 (46.3%)	3 (12.5%)	
LVEF (%), Me (Q1-Q3)		45.0 (38.0-48.0)	52.0 (47.8-54.3)	$p_1<0.01$
LAS (mm), Me (Q1-Q3)		43.0 (42.0-48.0)	40.0 (38.0-42.0)	$p_1<0.01$

Note:
p_1 – a statistically significant difference, according to the Mann–Whitney U test;
p_2 – a statistically significant difference, according to the Fisher exact test

Table 3 shows that patients with cognitive deterioration due to MoCA had statistically higher proportion of severe leukoaraiosis, lower LVEF and higher LAS. In the univariate logistic regression analysis as predictors for cognitive deterioration were Fazekas scale score > 3 points (OR 6.05; 95% CI, 1.56–24.47; p = 0.01), reduced LVEF (OR 0.84; 95% CI, 0.76–0.93; p<0.01), and increased LAS (OR 1.25; 95% CI, 1.08–1.45; p<0.01). The multivariate logistic regression analysis revealed that independent predictors for cognitive deterioration were Fazekas scale score > 3 points (OR 7.04; 95% CI, 1.14–43.52; p = 0.04), reduced LVEF (OR 0.88; 95% CI, 0.78–0.98; p = 0.03), and increased LAS (OR 1.26; 95% CI, 1.03–1.54; p = 0.03).

According to Table 4, patients with cognitive deterioration due to CDT had significantly older age, higher proportion of severe leukoaraiosis, lower LVEF and higher LAS. In the univariate logistic regression analysis, as predictors for cognitive deterioration were an increase in patients' age (OR 1.13; 95% CI, 1.02–1.25; p = 0.02), Fazekas scale score > 3 points (OR 3.30; 95% CI, 1.25–14.81; p = 0.02), reduced LVEF (OR 0.85; 95% CI, 0.77–0.93; p<0.01), and increased LAS (OR 1.26; 95% CI, 1.08–1.46; p<0.01). The multivariate logistic regression analysis revealed that independent predictors for cognitive deterioration were reduced LVEF (OR 0.90; 95% CI, 0.81–0.99; p = 0.04) and increased LAS (OR 1.19; 95% CI, 1.00–1.41; p<0.05).

Table 4 –Factors associated with cognitive deterioration according to CDT

Factor		Cognitive outcome		P
		deterioration	non-deterioration	
age (years), Me (Q1-Q3)		71.0 (69.0-73.0)	67.0 (63.0-69.0)	$p_1 = 0.01$
Fazekas scale (points)	<3, n (%)	22 (55.0%)	21 (84.0%)	$p_2 = 0.03$
	>3, n (%)	18 (45.0%)	4 (16.0%)	
LVEF (%), Me (Q1-Q3)		44.5 (38.0-48.0)	51.0 (48.0-54.0)	$p_1<0.01$
LAS (mm), Me (Q1-Q3)		43.5 (42.0-48.0)	40.0 (38.0-42.0)	$p_1<0.01$

Note:
p_1 – a statistically significant difference, according to the Mann–Whitney U test;
p_2 – a statistically significant difference, according to the Fisher exact test

As can be seen from table 5, patients with cognitive decline due to FAB had significantly higher proportion of severe leukoaraiosis, lower LVEF, and higher LAS. In the univariate logistic regression analysis as predictors for cognitive deterioration were Fazekas scale score > 3 points (OR 6.05; 95% CI, 1.56–24.47; p = 0.01), reduced LVEF (OR 0.88; 95% CI, 0.80–0.96; p<0.01), and increased LAS (OR 1.22; 95% CI, 1.06–1.41; p<0.01). The multivariate logistic regression analysis revealed that independent predictors for cognitive deterioration were Fazekas scale score > 3 points (OR 8.47; 95% CI, 1.54–46.51; p = 0.01) and increased LAS (OR 1.27; 95% CI, 1.04–1.54; p = 0.02).

Table 5 – Factors associated with cognitive deterioration according to FAB

Factor		Cognitive outcome		P
		deterioration	non-deterioration	
Fazekas scale (points)	<3, n (%)	22 (53.7%)	21 (87.5%)	$p_2 = 0.01$
	>3, n (%)	19 (46.3%)	3 (12.5%)	
LVEF (%), Me (Q1-Q3)		45.0 (38.0-50.0)	50.5 (46.8-54.0)	$p_1<0.01$
LAS (mm), Me (Q1-Q3)		43.0 (42.0-48.0)	40.5 (38.0-42.3)	$p_1<0.01$

Note:
p_1 – a statistically significant difference, according to the Fisher exact test;
p_2 – a statistically significant difference, according to the Mann–Whitney U test

The next step was the ROC analysis of significant quantitative predictors of cognitive deterioration revealed in univariate logistic regression analysis.

The results of ROC analysis of the statistically significant predictors of cognitive deterioration

As can be seen from Table 6, the predictive values of the patients' age are poor (the lower limits of AUC <0.6), whereas the predictive values of LVEF and LAS can be considered as worthless (the lower limits of AUC >0.6). According to the maximum values of the Youden index, the optimal cutoffs of LVEF for predicting cognitive deterioration ranged from 41% to 48%, depending on the cognitive scale used**.** The optimal cutoff of LAS for cognitive deterioration, according to all cognitive scales used, was the same: 42 mm.

DISCUSSION

Thus, according to all of the used cognitive scales, the same factors were independently associated with cognitive deterioration during the first year after ischemic non-lacunar strokes in patients with AF – severe leukoaraiosis, reduced LVEF, and increased LAS. Based on the ROC analysis, the optimal thresholds of LVEF values for predicting cognitive deterioration, depending on the cognitive scale, were within the interval of 41–48%. The optimal threshold of LAS for predicting cognitive deterioration, regardless of the scale used, was the same – 41 mm.

Generally, numerous studies have shown that leukoaraiosis is an independent risk factor for post-stroke CD. For example, in prospective study leukoaraiosis was independently associated with poorer cognitive outcomes at five years after stroke [15]. In large-scale multicenter study of patients with ischemic stroke, it was found a dose-dependent inverse

relationship between white matter hyperintensity volume and post-stroke cognitive functioning. This relation was independent of acute infarct volume, presence of old infarcts and lacunes, and infarct type [16]. The pathophysiological basis of post-stroke CD due to leukoaraiosis is poorly understood. A plausible explanation suggests that leukoaraiosis results in loss of microstructural integrity in white matter tracts, which impedes structural reorganization after stroke as well as reduced functional compensation through remote brain areas [17, 18]. The distinction of our study is that we are the first to demonstrate a relationship between the severity of leukoaraiosis and cognitive performance in the post-stroke period in patients with AF, and it is especially important that the study had a longitudinal design.

Table 6 – The results of ROC analysis of the statistically significant predictors of cognitive deterioration

Variable	Scale	Cut-off	AUC (95% CI)	Sensitivity, %	Specificity, %	The Youden index
age	MMSE	> 68	0.67 (0.54-0.78)	79.0	63.0	0.42
	CDT	> 68	0.68 (0.56-0.79)	80.0	68.0	0.48
LVEF	MMSE	≤ 42	0.76 (0.63-0.86)	50.0	96.3	0.46
	MoCA	≤ 48	0.77 (0.65-0.87)	78.1	70.8	0.49
	CDT	≤ 48	0.76 (0.64-0.86)	77.5	68.0	0.46
	FAB	≤ 41	0.72 (0.59-0.82)	41.5	100.0	0.41
LAS	MMSE	> 42	0.78 (0.66-0.87)	68.4	77.8	0.46
	MoCA	> 42	0.77 (0.64-0.86)	65.9	79.2	0.45
	CDT	> 42	0.77 (0.65-0.86)	65.0	76.0	0.41
	FAB	> 42	0.74 (0.62-0.84)	63.4	75.0	0.38

Regarding the relationships between echocardiographic parameters and cognitive performance, we have not yet found any studies that would examine this issue in patients with stroke, especially those with AF. Generally, to date, there are few studies on the associations between echocardiography and cognitive functioning. A prospective study involving older adults found that LAS was independently associated with decreased cognitive function [19]. Among community-dwelling older adults free of clinical dementia, lower cardiac output at study entry related to faster decline in cognition over the mean 3.5-year follow-up period [20]. In a study of AF patients without stroke, it was found that LAS was significantly higher and LVEF was considerably lower in patients with CD according to MoCA (< 26 points) than in patients without CD. Moreover, LAS had a significantly negative correlation, whereas LVEF had a significantly positive correlation with MoCA scores [21]. In another study, it was found significant associations of LVEF and LAS values with MoCA scores in patients with AF [16]. Up to now, it remains unknown how echocardiographic parameters can be associated with cognitive functions. There is an assumption that cardiac dysfunction leads to decreased ventricular blood output and sustained hypoperfusion of the brain, which damages neuron and glial cells and causes their subsequent demise, ultimately affecting cognitive functions [22].

Finally, it should be noted that our study's prospective design as well as revealed the optimal predictive thresholds of LVEF and LAS are of great practical importance for cognitive functioning prognosis in AF patients in the post-stroke period.

CONCLUSIONS

1. In AF patients during the first year after ischemic non-lacunar strokes, cognitive deterioration according to all used cognitive scales (MMSE, MOCA, CDT, and FAB) have the same independent predictors: severe leukoaraiosis (Fazekas scale >3) and echocardiographic parameters (decreased LVEF and increased LAS).

2. The optimal thresholds of LVEF for predicting cognitive deterioration are within the interval of 41–48%, depending on the scale used; the optimal threshold of LAS for predicting cognitive deterioration, irrespective of the scale used, was 41 mm.

PROSPECTS FOR FUTURE RESEARCH

It is necessary to study the effects of modified low LVEF on post-stroke cognitive functioning in AF patients.

AUTHOR CONTRIBUTIONS

The authors confirm their contribution to the paper as follows: study conception and design: M. Delva and N. Chekalina; data collection: V. Zayets; analysis and interpretation of results: M. Delva, N. Chekalina, I. Delva and V. Xayets; draft manuscript preparation: M. Delva, V. Zayets, N. Chekalina and I. Delva. All authors reviewed the results and approved the final version of the manuscript.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

ARTIFICIAL INTELLIGENCE DISCLOSURE

Artificial intelligence was not used in the paper preparation.

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