

Cardioembolic stroke in atrial fibrillation: challenges of prevention in clinical practice

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Objective. The aim of this study was to analyze the clinical characteristics of patients with atrial fibrillation (AF) and cardioembolic stroke (CES), to assess the quality of primary and secondary prevention of ischemic stroke (IS) in these patients, and to evaluate their short- and long-term prognosis.

Methods. A retrospective analysis of the medical records of inpatients treated for CES associated with AF between January 1 and June 30, 2023, was conducted at the neurovascular department of Ryazan City Clinical Hospital No. 11. Outcomes at 6 months were evaluated via a telephone survey, while 24-month outcomes were assessed using data from the “RT MIS” medical information system utilized at the hospital.

Results. A group of 117 patients was studied, comprising 41 (35.0%) men and 76 (65.0%) women. The mean age of the patients was 76.3±8.9 years. The vast majority of

the patients had comorbidities, and 18% had a history of recurrent stroke. Patients with permanent AF prevailed in the study group (41.9%). The in-hospital mortality rate was 35%. Prior to admission, all patients had a high risk of thromboembolic complications (mean CHA₂DS₂-VASc score 5.7±1.2), but only 10 of them (8.5%) received adequate anticoagulant therapy (ACT). Telephone survey results showed that 6 months after discharge, 25% of the patients were not compliant with recommendations for oral anticoagulants. At 24 months, out of 76 patients, 21 (27.6%) had died and 30 (39.5%) had been readmitted; of those readmissions, 25 (83.3%) were due to cardiovascular diseases and 5 (16.7%) were due to recurrent IS. During the 24-month follow-up, the risk of a fatal outcome in the ACT-compliant group was 9.1 times lower compared to the non-compliant group (OR=0.109; 95% CI: 0.034–0.353, p<0.001).

Conclusion. Patients with CES and AF are elderly individuals with a high incidence of comorbidities and a high risk of thromboembolic complications who do not receive adequate ACT in the outpatient setting. This patient category is characterized by high in-hospital (35%) and 2-year (27.6%) mortality rates. Adherence to ACT significantly reduces the risk of a fatal outcome within 24 months after the index event.

Keywords: atrial fibrillation, cardioembolic stroke, ischemic stroke, anticoagulation therapy, compliance.

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Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia and is associated with a significantly increased risk of ischemic stroke (IS). A history of AF is present in one in five IS cases [1]. The risk of developing AF increases with age, which in turn elevates the risk of cardiovascular events, primarily acute cerebrovascular events. Given the global trend of population aging, an increase in both AF incidence and the number of strokes can be expected in the future. Cardioembolic IS in patients with AF poses a significant challenge due to its severe course and high rates of disability and mortality [2]. The administration of anticoagulant therapy (ACT) is the cornerstone of preventing thromboembolic complications (TECs) in patients with AF [3]. However, despite taking anticoagulants, approximately one-quarter of these patients develop an IS or a transient ischemic attack (TIA), which raises many questions and requires further research [4].

Objective

The aim of this study was to analyze the baseline clinical characteristics of patients with AF and cardioembolic stroke (CES), to evaluate the quality of primary and secondary prevention of IS in these patients, and to assess their short- and long-term prognosis.

Methods

The study was conducted at the neurovascular department of Ryazan City Clinical Hospital No. 11. The medical records of 117 inpatients with CES and AF who received inpatient treatment from January 1 to June 30, 2023 were analysed. Inclusion criteria were: age 18 years and older, men and women with AF who

had suffered a CES. Demographic and socio-economic data, prior preventive treatment, clinical characteristics, comorbidities, and the results of laboratory and instrumental tests performed in accordance with stroke treatment standards were evaluated. Six months after discharge, a telephone survey was conducted to assess adherence to ACT and possible outcomes. At 24 months, outcomes were evaluated by analyzing data from the "RT MIS" medical information system used at the hospital; data were obtained for 100% of the study participants.

Statistical analysis

Statistical analysis was performed using StatTech v. 4.12.5 software (Stattech LLC, Russia). Continuous variables were tested for normal distribution using the Shapiro-Wilk test (for sample sizes of less than 50) or the Kolmogorov-Smirnov test (for sample sizes of more than 50). Normally distributed continuous variables were presented as the arithmetic mean (M) and standard deviation (SD). The 95% confidence interval (95% CI) was calculated to estimate the precision of the mean values. Non-normally distributed continuous data were presented as the median (Me) and the interquartile range (Q1–Q3). Categorical data were presented as absolute values and percentages. The 95% CIs for proportions were calculated using the Clopper-Pearson method. The comparison of proportions in the analysis of 2x2 contingency tables was performed using Fisher's exact test (when the minimum expected cell frequency was less than 10). The odds ratio (OR) with a 95% CI was calculated as a quantitative measure of the effect size when comparing categorical variables. Differences were considered statistically significant at $p < 0.05$.

Results

The study included 117 patients: 41 (35.0%) men and 76 (65.0%) women, with a mean age of 76.3 ± 8.9 years. All 117 patients suffered from arterial hypertension (AH), 89 (76.1%) had coronary heart disease (CHD), 36 (30.8%) had type 2 diabetes mellitus (DM), 25 (21.4%) had stage II–IV chronic kidney disease (CKD), and 113 (96.6%) had chronic heart failure (CHF). A history of recurrent IS was present in 18% of the patients. At the time of admission, only 46 patients (39%) were taking antihypertensive drugs, and 25 (21%) were taking lipid-lowering drugs. The in-hospital mortality rate was 35%. The main clinical and demographic characteristics of the patients are presented in Table 1.

Patients with permanent AF predominated in the study group (49 patients, 41.9%), while 39 patients (33.3%) had persistent AF, and 29 (24.8%) had paroxysmal AF. The mean CHA2DS2-VASc (5.7 ± 1.2) and HAS-BLED (2.2 ± 0.6) scores calculated prior to admission indicated that all patients required ACT; however, only 10 of them (8.5%) had been receiving the appropriate therapy in the correct dosage regimen before the cerebrovascular event occurred. The main reasons for the absence of anticoagulants in their treatment included: reluctance to take these medications (17 patients, 33.3%), high cost (13 patients, 25.5%), complaints about complications (6 patients, 11.8%), and the replacement of anticoagulants with antiplatelet agents (15 patients, 29.4%). Telephone survey results revealed that 6 months after discharge, 25% of the patients did not comply with oral

anticoagulant recommendations following their CES. At 24 months, 21 of the 76 patients (27.6%) had died, and 30 (39.5%) had been readmitted; of those readmissions, 25 (83.3%) were due to cardiovascular diseases and 5 (16.7%) were due to a recurrent IS.

ROC analysis demonstrated an association between in-hospital mortality and both the severity of the neurological deficit (NIHSS score > 12 points: AUC = 0.835; 95% CI: 0.751–0.918, $p < 0.001$) and the estimated glomerular filtration rate (< 52.3 mL/min/1.73 m² using the CKD-EPI formula: AUC = 0.661; 95% CI: 0.561–0.760, $p = 0.004$). The risk of in-hospital mortality was 4.4 times higher in patients with a history of myocardial infarction (95% CI: 1.660–11.701, $p = 0.003$). Over the 24-month follow-up, the risk of a fatal outcome was 9.1-fold lower in the ACT-compliant group compared to the non-compliant group (OR = 0.109; 95% CI: 0.034–0.353, $p < 0.001$).

Discussion

Between January 1 and June 30, 2023, 117 patients received treatment for CES associated with AF at the neurovascular department of Ryazan City Clinical Hospital No. 11; the majority of these patients were elderly or senile. Women predominated among the studied cohort, which aligns with data from foreign and domestic registries. This is attributed to the longer life expectancy of women compared to men in older age groups and, consequently, a higher incidence of stroke [1, 4–6]. Maksimova M.Yu. et al. also demonstrated a predominance of female stroke survivors over males in the age group of 70 years and older [7].

All patients with AF and CES were characterized by multiple comorbidities. AH was the most prevalent concomitant pathology and a significant risk factor for both AF and stroke. Notably, the majority of the patients were not receiving necessary hypotensive therapy at the time of CES onset. Consistent with many other studies, our patient cohort showed a high prevalence of CHD, CHF, CKD, and type 2 DM [5, 8]. For 18% of the patients, the current stroke was recurrent, which substantially increases the risk of unfavorable outcomes in this patient category. Comorbidities act as risk factors for both thromboembolic and hemorrhagic complications in patients with AF, making their assessment crucial when initiating ACT.

Patients with permanent AF prevailed in our cohort, which is consistent with findings by Melekhov A.V. et

Table 1. Clinical characteristics of patients with AF and CES

Variable	Patients included in the study	
	Number	%
Urban/rural, %	62/55	53/47
Employed/Unemployed, %	5/112	4.3/95.7
Disability, %	10	8.5
Active smokers, %	8	6.8
Alcohol abuse, %	4	3.4
Obese, %	48	41
BMI, kg/m ²	29.1±6.5	
Brachiocephalic arteries atherosclerosis (50%/50–70% stenosis)	89/41	76.1/35.0
NIHSS score	10.6±7.2	
Total cholesterol, mmol/L	5.1±1.4	
Triglycerides, mmol/L	1.31±0.9	
Glucose, mmol/L	6.7±2.7	
Creatinine, mmol/L	105.5±63	
Glomerular filtration rate, mL/min/1.73 m ²	56.2±17.1	

al., despite the risk of stroke being approximately equal for permanent and paroxysmal forms of AF. This may be explained by the fact that stroke is often the first clinical manifestation of previously undiagnosed AF. Therefore, the true prevalence of paroxysmal AF among patients with IS remains underestimated [1].

Prior to developing a CES, all patients had absolute indications for ACT due to a high risk of TECs; however, only a third of them were taking anticoagulants, and the vast majority of those did not adhere to the proper dosing regimen. A similar situation was described by Sokolov A.V. et al [9]. According to foreign authors, approximately 30% of patients with AF exhibit poor adherence to ACT [10]. An analysis of the reasons for the lack of direct oral anticoagulants (DOACs) in the treatment regimens of CES patients revealed that the overwhelming majority discontinued the drugs on their own due to low awareness of their condition and a lack of motivation. A survey by Potpara T.S. et al. demonstrated that even after a detailed explanation of the risk factors and benefits of therapy, 12% of patients would still refuse to take anticoagulants; the main reasons for refusal were fear of bleeding and underestimation of stroke risk [11]. The high cost of DOACs is another significant barrier to therapy; in our study, 25.5% of patients cited this as an issue.

Data regarding a history of stroke and adherence to ACT are controversial. On one hand, due to post-stroke cognitive impairment, patients often forget to take their medications or fail to recognize the need for therapy, as demonstrated by Tiili P. et al [12]. On the other hand, Luger S. et al. reported high adherence (>90%) to ACT during the first year after a stroke [13]. In our study, 75% of the patients adhered to ACT recommendations following a CES, which is significantly higher than the percentage of patients taking

DOACs for primary TEC prevention. This is likely due to an increased awareness of the problem by both the patients and their relatives. Among all IS subtypes, CES is associated with the highest acute in-hospital mortality and a rather poor long-term prognosis. In a study by Arboix A. et al., in-hospital mortality for CES was 27.3%, compared to 0.8% for lacunar and 21.7% for atherothrombotic strokes [14]. In-hospital mortality in our sample was even higher (35%), which can be attributed to insufficient control of cardiovascular risk factors at the pre-hospital stage and delayed hospital admission. Regarding long-term prognosis, several authors report that the 24-month mortality rate for AF patients after a CES ranges from 30% to 50%, with the lack of adequate ACT being the leading modifiable risk factor [10, 14, 15]. In our cohort, the 2-year mortality rate was 27.6%, and adherence to ACT significantly reduced this risk.

Conclusion

Patients who experience a CES associated with AF form a particularly vulnerable cohort of elderly individuals with multiple comorbidities, which results in a high risk of recurrent thromboembolic events. Adequate ACT prior to the cerebrovascular event is received by only 8.5% of patients; however, even after suffering a CES, only 75% of them remain compliant with the prescribed direct oral anticoagulant regimen. CES in patients with AF is characterized by high rates of in-hospital mortality (35%), 2-year mortality (27.6%), hospital readmissions (39.5%), and recurrent IS (16.7%). Uninterrupted ACT reduces the risk of a fatal outcome within 24 months of the index event by a factor of 9.1.

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