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### Original research article

## The importance of atrial fibrillation and selected echocardiographic parameters for the effectiveness and safety of thrombolytic therapy in patients with stroke

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#### ABSTRACT

*Background*: The efficacy and safety of thrombolytic therapy in stroke depend on multiple factors. The aim of this study was to evaluate the significance of atrial fibrillation the prognosis in terms of the functional status in patients with stroke treated with intravenous thrombolysis. An additional aim was also to assess the potential significance of reduced ejection fraction (EF) and enlarged left atrium (LA) of the heart for the prognosis in patients with stroke who underwent thrombolytic therapy.

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*Methodology:* A prospective study involved enrollment of 222 patients, mean age of 72 years with first-in-life ischemic stroke. In all participants there were realized procedures as follows: neurological status before administering rt-PA (NIHSS), selected echocardiographic parameters, functional status on the 14th day from the onset (mRankin scale) and analysis the bleeding events.

Results: Atrial fibrillation was significantly more frequent in women than men; females had higher CHA2DS2VASc scores and heavier neurological conditions on day 1 of stroke. Two independent factors for poor prognosis (3–5 points by mRankin) were found: the NIHSS score and the CHA2DS2VASc score  $\geq$ 3. We identified 2 independent factors for death within 14 days from the onset: the result by NIHSS and the EF. The NIHSS score turned out to be the only independent predictor of hemorrhage during hospitalization: RR 1.19; CI [1.06–1.33]; p = 0.003; p for model = 0.0025.

Conclusions: The presence of atrial fibrillation worsens the patient's prognosis in terms of the functional status and survival during the acute period of stroke in patients treated with intravenous thrombolysis.

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Higher NIHSS and CHA2DS2VASc scores and reduced EF in patients with stroke treated with thrombolysis are the predictors of unfavorable short-term prognosis.

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### 1. Background

The efficacy and safety of thrombolytic therapy in stroke depend on multiple factors. Although the potential importance of atrial fibrillation (AF) for the above parameters has been the subject of several studies, a disparity between their results prevents us from formulating a clear conclusion. It is likely that both the type of atrial fibrillation and coexisting structural and functional heart disorders accompanying arrhythmia may play a role regardless of the electromechanical and hemodynamic effects associated with AF. Given the prevalence of AF among patients with stroke, one should define the meaning of arrhythmia for the effects of thrombolytic therapy, as it may affect the selection of patients who could obtain the best benefits from such treatment.

The aim of this study was to evaluate the significance of AF for the prognosis in terms of the functional status in patients with stroke treated with intravenous thrombolysis. An additional aim was also to assess the potential significance of reduced ejection fraction (EF) and enlarged left atrium (LA) of the heart for the prognosis in patients with stroke who underwent thrombolytic therapy.

### 2. Methodology

A prospective study (period: 2014–2015) involved enrollment of 222 patients, mean age of 72 years (39–89; 107 women, 155 men); the subjects were patients with first-in-life stroke diagnosed by the WHO's clinical criteria, and an ischemic focus in the brain present in neuroimaging (CT and/or MRI of the head) [1]. All the subjects received recombinant tissue plasminogen activator (rt-PA) intravenous within 4.5 h from the disease onset, which was in accordance with the eligibility criteria for thrombolytic therapy [2]. The study excluded the patients who underwent endovascular treatment due to cerebral stroke – the aim of the study was to evaluate the importance of selected parameters for the prognosis of patients treated homogeneously (without the effect of general anesthesia used in approximately half of the patients given endovascular treatment in our center).

All the patients included in the study were examined in terms of the following:

- the patient's age at the time of first-ever ischemic stroke;
- presence of atrial fibrillation (valvular and non-valvular); AF due to reasons other than valvular heart disease was considered as non-valvular atrial fibrillation;
- presence of conditions/comorbidities such as arterial hypertension, diabetes and lipid disorders; >70% of atherosclerotic carotid artery stenosis (ipsilaterally to the ischemic focus in the brain);

- neurological status evaluated before administering rt-PA according to NIHSS (National Institutes of Health Stroke Scale) [3];
- anticoagulant therapy conducted before the stroke onset;
- result by the CHA2DS2VASc scale;
- selected echocardiographic parameters: the presence of thrombus in the left atrium, reduced EF (<55%) and enlarged left atrium (LA > 3.8 cm for women and >4.0 cm for men relative to body surface area);
- intracranial bleeding
- extracranial bleeding: from the nasal cavities, gastrointestinal tract, genital and urinary tract or from other areas requiring substitution with 2 units of packed red blood cells;
- functional status on the 14th day from the onset according to mRankin scale [4].

The diagnosis of hypertension was consistent with the recommendation by the Polish Society of Cardiology [5]; diabetes mellitus was diagnosed according to the criteria by the Polish Diabetes Association (2013) [6]; dyslipidemia was defined as total cholesterol serum level >200 mg/dl (>5.18 mmol/l); or LDL-cholesterol serum level >100 mg/dl (2.59 mmol/l); or HDL-cholesterol serum level <35 mg/dl (0.91 mmol/l); or triglycerides serum level >135 mg/dl (1.53 mmol/l).

The degree of common carotid artery stenosis and/or internal carotid stenosis was rated according to the NASCET criteria [7].

Patients were divided into 2 groups depending on the presence of AF (present vs. absent) and depending on the CHA2DS2VASc result (<3 vs.  $\geq$ 3 points); results were compared in parallel groups.

The type of intracranial bleeding was determined according to the ECASS I and II definition (European Cooperative Acute Stroke Study) [8,9].

Multivariate analysis was performed in order to determine independent factors for unfavorable prognosis defined as obtaining 3–5 points on mRankin scale by a patient on their 14th day after stroke or as the patient's death within 14 days of onset. The analysis included the following parameters: age (also in subgroups: <65 years and  $\geq$ 65 years), sex (including subgroups: <65 years and  $\geq$ 65 years), arterial hypertension, diabetes, atrial fibrillation (valvular and non-valvular AF), lipid disorders, stenosis of the carotid artery >70%, NIHSS, CHA2DS2VASc  $\geq$ 3, EF < 55%, enlargement of LA and bleeding during 14-days hospitalization.

### 3. Results

Demographic and selected clinical patients' parameters are presented in Table 1.

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