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Original research article

Cerebral thrombolysis in patients with ischemic stroke and heart failure

Piotr Sobolewski^{a,b,*}, Grzegorz Kozera^c, Wiktor Szczuchniak^b,
Anna Sobota^b, Kamil Chwojncki^d, Marcin Gruchala^e, Walenty M. Nyka^d

^a The Faculty of Medicine and Health Sciences, Jan Kochanowski University, Kielce, Poland

^b Department of Neurology and Stroke Unit, Holy Spirit Specialist Hospital in Sandomierz, Poland

^c Department of Neurology, Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University, Toruń, Poland

^d Department of Neurology, Medical University of Gdańsk, Poland

^e First Department of Cardiology, Medical University of Gdańsk, Poland

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ABSTRACT

Background: Heart failure (HF) is common among patients with ischemic stroke (IS), however its impact on outcome after iv-thrombolysis has not been fully determined. Moreover, definition of HF has been recently modified, but majority of stroke studies classified patients regarding an old HF criteria. Thus, the aim of our study was to evaluate the relationship between both, newly and formerly defined HF and the long-term outcome, mortality and the presence of hemorrhagic complications in patients with acute IS treated with iv-thrombolysis.

Methods: We retrospectively evaluated data from 328 Caucasian patients with IS consecutively treated with iv-thrombolysis. HF was defined according to old and new definition; long-term outcome was assessed with modified Rankin Scale (mRS) score and mortality rate on 90th days after IS.

Results: The incidence of HF did not differ between patients with favorable (mRS 0–2) and unfavorable (mRS 3–6) functional outcome respectively for the old and for the new definition (10.4% vs. 15.5, $p = 0.17$; 17.4% vs. 18.1%, $p = 0.88$) and between those who survived and died within 90 days after IS (11.7% vs. 20.0%, $p = 0.27$; 17.2% vs. 25.0%, $p = 0.38$, respectively). Multivariate analysis showed no impact of HF diagnosis on outcome ($p = 0.94$) or mortality ($p = 0.64$).

Conclusion: The presence of systolic HF, defined according to an old and a new definition, does not determine safety and efficacy of cerebral iv-thrombolysis in patients with IS.

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* Corresponding author at: The Faculty of Medicine and Health Sciences, Jan Kochanowski University, 19 IX Wieków Kielc Str., 25-217 Kielce, Poland.

E-mail address: piotrsobolewski@poczta.onet.pl (P. Sobolewski).

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1. Introduction

Heart failure (HF) is a risk factor for ischemic stroke (IS) that is present in approximately 1–2% of the population. Factors that predispose to thromboembolic events with HF include low cardiac output, with relative stasis of blood in dilated cardiac chambers, poor contractility, and regional wall motion abnormalities. The risk of stroke increases with decreasing left ventricular ejection fraction (LVEF), even after adjusting for other stroke risk factors [1–3]. HF is found in 10–24% of acute stroke patients and is associated with poor outcome and increased mortality in IS [4–7]. The most frequent causes of IS in patients with HF are: thrombus formation due to impaired left ventricular contractility and atrial fibrillation (AF), increased aggregation of thrombocytes and reduced fibrinolysis [8–10].

Intravenous cerebral thrombolysis (iv-thrombolysis) with rt-PA is effective medical therapy for acute IS, but its widespread implementation is limited by a high number of contraindications and relatively short time window [11]. Moreover, its safety and efficacy is influenced by the patient's age, severity of initial deficit, presence of hemorrhagic complications and a number of other factors [12–15].

A cardiogenic etiology, which is present in 22–39% of ischemic strokes, may determine the safety and efficacy of iv-thrombolysis [16,17]. Numerous reports have demonstrated the negative impact of atrial fibrillation (AF) on the long-term outcome of iv-thrombolysis [8,18,19]. Inversely, data on the outcome after cerebral thrombolysis in patients with HF are sparse. Moreover, available reports concern heterogeneous groups of patients, treated with both intra-arterial and iv-thrombolysis, within a wide range of time windows, and mostly do not include assessment of the left ventricular ejection fraction (LVEF) in the protocol [20,21]. A single study, based on the Polish stroke patients, showed that low LVEF is an independent factor for death within 14 days after thrombolytic therapy [22]. Moreover, since the definition of HF has been modified in 2016, little studies concerned an impact of newly defined HF on stroke outcome. Thus, it still remains unclear if cerebral iv-thrombolysis is similarly safe and efficient in IS patients with HF as in IS patients without HF.

Therefore, we aimed to evaluate the relationship between the presence of systolic HF, diagnosed on the basis of the patient's history and echocardiographic parameters, and the safety and efficacy of iv-thrombolysis in routine practice.

2. Methods

2.1. Study design and patients

We retrospectively evaluated the demographic and clinical data of Caucasian patients with IS who were consecutively treated with iv-thrombolysis from January 2008 to January 2013 in the Department of Neurology and Stroke Unit of the Holy Spirit Specialist Hospital in Sandomierz, Poland. Patients' records were collected from the Pomeranian Stroke

Register (PRUM), which is an open, multi-center, internet-based consecutive stroke register [23]. Data from patients treated >4.5 h from stroke onset, those with combination therapy (intravenous plus intra-arterial thrombolysis) were excluded.

The Department of Neurology and Stroke Unit of the Holy Spirit Specialist Hospital in Sandomierz is recognized as a stroke unit according to the Polish national criteria and is equipped with appropriate monitoring and diagnostic facilities [24]. The stroke unit provides a 24-h stroke service 7 days a week. All patients were examined at the time of admission by a stroke physician, and the severity of stroke symptoms was assessed using the National Institutes of Health Stroke Scale (NIHSS) [25]. Stroke was diagnosed on the basis of the ICD 10 criteria and was confirmed on discharge by clinical evaluation and neuroimaging. Cerebral thrombolysis with the intravenous infusion of recombinant tissue plasminogen activator (rt-PA) was administered according to current guidelines [11, 27,28].

All blood samples were routinely taken at the time of admission and the results of biochemical analyses were obtained before starting iv-thrombolysis. Brain computed tomography (CT) scans were performed in all patients upon admission to hospital and between 22–36 h after iv-thrombolysis. In selected cases, especially in the case of hemorrhagic complications, additional CT scans were performed according to the patient's status and clinical indications. Brain magnetic resonance imaging (MRI) was not routinely performed.

The 90-day stroke outcomes were measured using the modified Rankin scale (mRS) [26]. A favorable outcome was defined as mRS score ≤ 2 points, while an unfavorable outcome was defined as an mRS of 3–6 points. Hemorrhagic transformation (HT) and symptomatic intra-cerebral hemorrhage (SICH) rates were assessed according to the European Cooperative Acute Stroke Study (ECASS) II criteria [29].

2.2. Cardiovascular assessment

A basic cardiological assessment was performed in all patients treated with iv-thrombolysis including electrocardiography (ECG) on admission, 3-day continuous ECG monitoring and blood pressure and transthoracic echocardiography (TTE) performed during the first day of hospitalization. TTE was performed according to guidelines applicable until 2013 [30]. Systolic heart failure was recognized according both, to the old criteria when patients' complaints were categorized as class II–IV according to the New York Heart Association functional classification (NYHA) [31] before hospitalization and concomitant reduction of the LVEF below 45% was detected by TTE (LVEF moderately and severely abnormal) [30] or based on previous diagnosis in medical records and according to the new criteria in which, apart from additional factors, HF with preserved, mid-range and reduced ejection fraction was diagnosed [32].

The ethics committee approved all data analyses (Ethics Committee of Świętokrzyska Medical Chamber), and all patients treated with iv-thrombolysis were reported to the SITS registry.

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