Outcomes of intravenous thrombolytic therapy in cardioembolic strokes

Mustafa Çetiner 1, Murat Seyit 1, Neslihan Eskut 2, Gönül Akdağ 1, Fatma Akkoyun Arıkan 1, Sibel Canbaz Kabay 1

1 Department Of Neurology, Kütahya Health Sciences University, Kütahya, Turkey
2 Department Of Emergency Medicine, Pamukkale University, Denizli, Turkey
3 Department Of Neurology, University Of Health Sciences, İzmir, Turkey

Corresponding Author
Mustafa Çetiner
E-mail: dcketiner76@gmail.com

The authors declared that this study has received no financial support.

Published
2021 February 19

Keywords: Acute ischemic stroke, Cardioembolic stroke, Intravenous thrombolytic therapy

Abstract

Background/Aim: It is controversial whether intravenous recombinant tissue plasminogen activator (IV r-TPA) treatment outcomes in cardioembolic strokes differ from other types of strokes. This study aims to investigate the clinical data of patients with cardioembolic and large-vessel atherosclerosis who received IV r-TPA treatment and compare and discuss the results according to the literature.

Methods: The data of the patients who were admitted within the first 4.5 hours following the onset of symptoms, diagnosed with acute ischemic stroke in the Neurology clinic of Kütahya Evliya Çelebi Training and Research Hospital and underwent IV r-TPA were evaluated in this retrospective cohort study. Demographic data, clinical and functional results of patients were compared between the two groups (cardioembolic and large vessel atherosclerosis).

Results: Eighty-five patients with ischemic stroke who received IV r-TPA treatment due to cardioembolism and large-vessel atherosclerosis were included in the study. There were 51 patients (60%) in the cardioembolic stroke group and 34 patients (40%) in the large vascular atherosclerotic group. There was no significant difference in terms of functional results between the groups (62.7% vs 44.1%; \(P=0.09\)). While symptomatic intracerebral hemorrhage was not detected in the large-vessel atherosclerosis group, it occurred in 3.9% of the cardioembolic stroke group.

Conclusion: This study proved that functional and clinical results are similar between cardioembolic and large-vessel atherosclerosis patients who were treated with IV r-TPA treatment. Regardless of the etiology, all suitable patients with acute ischemic stroke should be treated with thrombolytic therapy.
Introduction

Ischemic stroke is subdivided according to etiological causes and has different prognosis and mortality rates based on the mechanisms of its formation [1,2]. It has been reported that intravenous recombinant tissue plasminogen activator (IV r-tPA), the basis of intravenous thrombolytic therapy in acute ischemic stroke, improves functional results in all strokes [3,4]. However, the response to IV r-tPA treatment may vary depending on the size, content and the source of the clot. While thrombus formed under slow blood flow in the heart cavities is rich in fibrin, that formed under fast blood flow in atherosclerotic-stenotic lesions is rich in thrombocytes. Therefore, it is assumed that the response to fibrinolytic agents such as tissue-type plasminogen activator will be superior in heart-induced embolism [5]. Studies investigating functional results of intravenous thrombolysis in patients with cardioembolic stroke are contradictory in the literature. In the study of Molina et al. [6], early recanalization following thrombolysis was more frequent, faster, and higher in cardioembolic patients with middle cerebral artery infarction, and the improvement in the three-month period was better in non-cardioembolic strokes in the study of Rocha et al. [7]. On the other hand, in the study of Nam et al., the rate of full recanalization was lower in cardioembolic strokes, the rate of poor functional recovery in the third month was higher, and heart-borne embolism was an independent determinant for the poor functional result in the third month [8]. Similarly, in the study of Kimura et al., patients with atrial fibrillation (AF) who underwent IV thrombolysis in acute ischemic stroke had worse clinical results compared to the ones without AF [9].

On the other hand, in a study reported from our country, functional results were not different in the 3rd month after thrombolytic therapy in patients with acute middle cerebral infarction of different stroke types [10].

The aim of this study is to examine, compare and discuss the results of acute ischemic stroke patients undergoing IV thrombolytic therapy with cardioembolism and large vessel atherosclerosis according to TOAST classification.

Materials and methods

The data of the patients who were admitted to the emergency department within the first 4.5 hours following the onset of symptoms, diagnosed with acute ischemic stroke and underwent IV r-tPA at Kütahya Evilya Celebi Training and Research Hospital Neurology Department between May 2014 and September 2018 were evaluated retrospectively. Thrombolytic treatment decision was made according to AHA / ASA 2013 [11] and 2016 [12] guidelines. All patients were given an intravenous bolus of 10% of the total dose of 0.9 mg / kg (maximum 90 mg) of r-tPA (alteplase®) and the rest was administered as hourly infusion. Ischemic stroke risk factors, demographic and clinical features, neurological examination findings, results of hemogram and biochemistry tests, and symptom needle (SN) time were recorded from patient files. The patients’ evaluation was based on the etiological classification of Acute Stroke Treatment [13] (TOAST) in Trial of Stroke Org 10172. Eighty-five patients with cardioembolic and large vessel atherosclerosis were included in the study. The computed brain tomography images of the patients were examined before and during IV r-tPA, or intracranial bleeding. The presence of hemorrhagic infarction with more than 30% of the infarct area accompanied by neurological deterioration, intracranial hemorrhages causing an increase of more than 4 points in NIHSS or death were called symptomatic intracerebral hemorrhage (sICH), while those detected incidentally in control imaging were called asymptomatic intracerebral hemorrhage (aICH) [14]. Intracranial bleeding occurring within the first 36 hours of treatment was considered r-tPA complication. The pre-post-treatment neurological disabilities of the patients were evaluated with the national Health Institutes of Health Stroke Scale (NIHSS) scores and the 3rd month neurological disabilities, with modified Rankin Scale (mRS) scores.

Early neurological improvement (ENI) was defined as a NIHSS score of 0 to 1 24 hours following thrombolytic therapy or an improvement in the NIHSS score of ≥8 points (14). Having mRS ≤2 at 3 months was considered a good functional result, and mRS ≥2, a poor one [15].

The study was approved by the Dumlupinar University of Local Ethics Committee (Date: 14/11/2018, Decision no: 2018/14-8).

Statistical analysis

Statistical analyses were performed using SPSS 24.0 (IBM Corp.; Armonk, NY, USA) program. Normally distributed variables were presented as mean (standard deviation), and non-normally distributed variables were presented as median (minimum-maximum). In the comparison between the independent groups, t-test was used for the parametric data and Mann-Whitney U test was used for the non-parametric data. The difference between the categorical data was evaluated by chi-square and Fisher's exact test. P-value <0.05 was considered statistically significant.

Results

Demographic and basic features of patients

The study included eighty-five patients with cardioembolic and large vessel atherosclerosis who were diagnosed with acute ischemic stroke and underwent IV-r tPA. Forty-eight were male (56.5%) and thirty-seven were female (43.5%) and their mean age was 70.32 (10.39) (range, 35-88) years.

Two groups were formed with fifty-one patients in the cardioembolic stroke (60%) group and thirty-four patients in the large vessel atherosclerosis (40%) group. Among vascular risk factors, smoking was more prevalent in the large vessel atherosclerosis group (P=0.03), while coronary artery disease (CAD) and atrial fibrillation (AF) were more common in the group with large vessel atherosclerosis (P<0.001). The two groups were similar in terms of age, gender, SN time, initial NIHSS score averages, glucose levels, systolic and diastolic blood pressure mean values. There was no significant difference in mean platelet volume (MPV) and platelet averages between the groups. Demographic and basic characteristics of the patients and the statistical comparison between them are presented in Table 1.
Discussion

IV thrombolysis is the main treatment for acute ischemic stroke and effective in all stroke subtypes [3]. Different subtypes of ischemic stroke have different risk factors, clinical features, pathogenesis, and prognosis [16,17]. In earlier studies, it was investigated whether clinical results after thrombolysis differed from other stroke types in cardioembolic strokes, but contradictory results were obtained [7,18,19]. In this study, 3-month clinical and functional results were compared in patients with cardioembolic and large-vessel atherosclerosis following IV thrombolysis treatment, and no significant differences were observed.

Theoretically, cardioembolic thrombi are rich in fibrin and erythrocytes than atherosclerotic thrombi, which are more organized and richer in platelet. Thrombolytic treatment responses are expected to differ according to the structural composition of the thrombus, and thrombi of cardiac origin will be more prone to dissolution with intravenous alteplase. In this context, a study in which recanalization following IV thrombolysis was monitored with transcranial doppler showed that recanalization in patients with cardioembolic stroke was more frequent, faster and more complete than other stroke subtypes in patients with middle cerebral artery occlusion [6].

There are studies emphasizing that cardioembolic strokes are associated with poor results and high mortality [8,20]. In MRI-based studies of Schmitz et al. [19], earlier neurological recovery and better functional outcome (mRS: 0,1) were achieved following IV-tPA treatment in patients with cardioembolic stroke compared with stroke due to large vessel atherosclerosis. Similarly, in the study of Vaclavik et al. [14], compared to atherothrombotic strokes, the likelihood of symptomatic intracranial hemorrhage was low in cardioembolic strokes, and early neurological healing, increased 3-month good functional clinical outcome (mRS: 0,1), and indifferent mortality rates were observed. ENI is a strong determinant of positive functional results in 3 months in patients with acute ischemic stroke after thrombolytic therapy [21]. In the study of Fuentes et al., no significant difference was found between ENI and 3-month functional results in stroke subtypes, as in this study [22]. In accordance with the present study, no difference was found between the two groups in terms of ENI, 3-month good functional outcome, intracerebral hemorrhage and mortality.
Patients with cardioembolic stroke have a higher risk of hemorrhagic transformation [18,23,24]. Wang et al. [18] reported that this may decrease the benefit of thrombolytic therapy. In this study, symptomatic intracerebral hemorrhage was higher in patients with cardioembolic stroke after thrombolysis, and worse clinical results were obtained at 3 months follow-up compared to stroke patients with large vessel atherosclerosis. It has been reported that patients with AF have a higher risk and poor prognosis in terms of intracerebral bleeding following thrombolysis [25,26]. In this study, the rate of patients with AF and intracerebral bleeding rates were significantly higher in the cardioembolic stroke group. In a study investigating the frequency of hemorrhagic transformation in ischemic stroke and related factors, the size of AF and infarct area were independent risk factors, but no relationship was found between the 3rd month prognosis and hemorrhagic transformation [27]. In the report of Dang H et al., hemorrhagic transformation following the treatment was significantly higher in patients with AF undergoing IV thrombolysis, while no correlation was detected with prognosis [28]. Similarly, in a large-scale metaanalysis study involving Chinese patients, Wen L., et al. stated that hemorrhagic transformation was significantly higher in patients with AF who underwent IV thrombolysis [29]. In our study, there was no significant difference between symptomatic and asymptomatic intracerebral bleeding rates and functional results between the two groups.

Limitations

The limitations of this study include its retrospective and single-center design, as only few patients with cardioembolic and atherothrombotic stroke were admitted. Therefore, etiologically, patients with cardioembolic stroke could not be compared with other stroke subtypes except for large vessel atherosclerotic stroke.

Conclusion

Thrombolytic therapy should be applied to all suitable acute ischemic stroke patients, regardless of the etiology. Sharing these results in terms of the spread of IV-r tPA in our country is valuable.

References