# Thrombolytic or endovascular therapy for acute ischemic stroke: Time is brain

Acute occlusion of the cerebral artery leads to time-dependent ischemic brain tissue damage. If the artery is not opened urgently, the ischemic process worsens, leading to tissue death and consecutive cerebral infarction. The most important determinants of the quality of life as well as life expectancy of stroke survivors are time of recanalization, ischemic area, and collateral circulation patency. At the moment, the only approved treatment for acute ischemic stroke is intravenous (IV) recombinant tissue plasminogen activator (tPA) administered within the first 3 hours after symptom onset. When given IV, tPA initiate very fast intra-arterial thrombus dissolution. This early but very often only partial recanalization can lead to ischemic tissue rescue and subsequent clinical recovery. Unfortunately, less than 5% of patients with ischemic stroke receive IV tPA and only 30 to 40% of treated patients achieve early recanalization, that is complete and sustained in less than 20% of patients.[1]

In Europe, 3 hours time window for thrombolytic therapy for acute ischemic stroke has been extended to 4.5 hours according to recommendations from the European Cooperative Acute Stroke Study III.[2]

Carotid and transcranial ultrasonography in acute stroke represent noninvasive methods that allow early recognition of the stroke subtype, etiology, and clinical prognosis at the bedside. With this procedure, information about vessel patency and the status of collateral circulation can be obtained in real time, allowing better selection of patients who could benefit from more aggressive endovascular reperfusion therapies.[3]

During the last years, various endovascular intra-arterial approaches have been developed for treating patients with acute ischemic stroke, particularly those presenting with severe neurological deficits. Prospective, but usually non-randomized clinical studies showed significantly higher recanalization rates (up to 85%) for large-vessel occlusion stroke with intra-arterial endovascular approaches than with intravenous thrombolysis.

Recently published data on thrombolysis in acute ischemic stroke, as an experience from the tertiary care center in India, further emphasized the significance of extracranial and intracranial vessels examination either with neuroimaging methods (CT or MR angiography) or with sonography methods. Authors showed that patients with acute ischemic stroke and large vessels occlusion with no evidence of cross flow through circle of Willis collaterals benefit more from endovascular treatment in comparison with systemic trombolysis.[4]

Although patients treated in this study with IV tPA and endovascular therapy had similar National Institutes of Health Stroke Scale (HIHSS) scores, the median modified Rankin Scale (mRS) in the endovascular group was 0.5 as compared to the intravenous group which was 3 and this difference was found to be statistically significant. On the other side, it also seemed that complete and/or sustained recanalization was also statistically significantly more frequent in the endovascular group (82% of patients had a mRS of 2 or less at 90 days in the endovascular group as compared to 44% in the intravenous group). The mortality rates remained similar between the two groups.[4]

Clinical efficacy of intravenous thrombolysis and its ability to achieve successful sustained recanalization are limited in patients presenting with acute stroke due to large-vessel occlusion (internal carotid artery, proximal middle cerebral artery, vertebral and basilar artery).

This observation was confirmed in the study of Huded and coworkers.[4] Namely, patients who underwent intravenous thrombolysis with documented large vessel disease, with no cross flow on angiogram (insufficient collateral circulation), had less favorable early and delayed outcome as compared to patients treated with endovascular modalities.


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In patients treated within 4.5 hours of symptom onset, the endovascular group had a better outcome compared to intravenous group with documented large vessel disease.

The main advantages of intravenous thrombolysis over intra-arterial endovascular treatment strategies include low cost, simple mode of application, and rapid administration after completion of basic laboratory testing and exclusion of hemorrhage on non-contrast CT scanning of the head. Knowing that time is crucial for brain tissue rescue in acute arterial occlusion; another advantage of intravenous thrombolytic therapy is that it is time saving. That was also confirmed with the results of the present study. Authors showed that the "door to needle" time in the endovascular group was significantly longer (218 minutes) compared with the IV tPA group (137 minutes).[4]

Results of the present study from the tertiary care center in India[4] again stressed out controversial questions about treatment modalities of acute ischemic stroke. Unanswered questions remaind: Which subgroup of patients should be treated with intravenous thrombolysis, which population of patient benefit from the "bridging therapy," and which group of patients with acute ischemic stroke are the best candidates for endovascular treatment.

Another unresolved issue is the type of device for endovascular treatment and time window for endovascular treatment of acute ischemic stroke.

As authors discussed,[4] the results of several studies that included either insufficient number or poorly selected patients with acute ischemic stroke treated with different endovascular devices did not answer the above mentioned questions. Results of the MERCI,[5] Multi Merci,[6] and Penumbra[7] trials showed better recanalization rates and outcome in patients with acute ischemic stroke having associated large vessel occlusion who were treated with different endovascular devices.

On the other side, three recent randomized trials-Interventional Management of Stroke (IMS) III, Mechanical Retrieval and Recanalization of Stroke Clots Using Embolectomy (MR RESCUE), and Synthesis Expansion: A Randomized Controlled Trial on Intra-Arterial Versus Intravenous Thrombolysis in Acute Ischemic Stroke (SYNTHESIS Expansion) evaluated the efficacy of endovascular treatment of acute ischemic stroke failed to demonstrate any significant clinical benefit of endovascular therapies. These findings raised concerns and questions in the medical community regarding the future of endovascular treatment for acute ischemic stroke and still remained many unanswered questions regarding acute ischemic stroke treatment.[8]

These trials confirmed a strong association between successful, sustained recanalization and revascularization and improved clinical outcomes. Lesson that we learned from all the studies investigated either endovascular or thrombolytic therapy is that the most important goal is to achieve rapid reperfusion and to minimize delays from symptom onset to reperfusion time.

The trials demonstrated similar safety profiles of intravenous and intra-arterial reperfusion strategies, including rates of intracranial hemorrhage.[8]

We also have learned that evaluation for large-vessel occlusion with noninvasive imaging is currently recommended for all patients with acute ischemic stroke who are potential candidates considered for urgent endovascular reperfusion therapies.

Further large randomized trials with highly selected patients are needed, to answer the questions regarding appropriate selection of patients for endovascular or thrombolytic therapy.

All attempts should be made to minimize delays from stroke symptom onset to achievement of successful reperfusion, because time is crucial, time is brain.

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