

## TIME IS BRAIN - EARLY RECANALIZATION IN ACUTE ISCHEMIC STROKE

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Stroke is the third leading cause of death in America and the number one cause of adult disability. Prompt diagnosis and treatment are imperative to increase the odds of a good outcome.

Even though stroke is not a common complication of catheter angiography, when it occurs, it is associated with a high morbidity and mortality (1-2). Several mechanisms have been proposed to account for the neurologic complications of catheter angiography. The most common cause implicated is thromboembolism, due to thrombi formation inside the catheter or disruption of an atherosclerotic plaque by the catheter or guide wire. Catheter-related arterial dissections, platelet activation, and neurotoxicity of contrast agents are other potential etiologies (1-3).

When facing a patient with signs and symptoms suggestive of an acute ischemic stroke, prompt evaluation of the intra and extracranial vessels for determination of the culprit artery involved as well as establishment of the potential mechanism of the stroke should be pursued (4). New techniques of magnetic resonance imaging and computed tomography, can quickly assess the patient, evaluate early ischemic changes, reveal hypoperfusion/ischemic penumbra, and locate the site of vessel occlusion, stratifying and selecting those patients that will benefit most from reperfusion (5-6).

Even though spontaneous recanalization can occur in one-quarter of patients within the first 24 hours and up to 52.7 % of cases up to 1 week after the stroke, only early recanalization within the first 6 hours have positively correlated with a good clinical outcome in patients with acute ischemic stroke (7). Therefore, early recanalization therapy with the use of fibrinolytic agents and/or mechanical thrombolysis should be

pursued in an attempt to re-establish the cerebral blood flow and salvage of the threatened tissues. A National Institute of Neurological Disorders and Stroke compliant strategy (ie, evaluation by emergency physician <10 minutes after arriving at the hospital, interpretation of CT scans <45 minutes, and administration of tPA <1 hour after initial assessment) renders a substantial clinical gain, with the number of patients needed to treat for benefit of  $\approx 3.2$ , that is, for every 1000 patients treated,  $\approx 323$  will attain a better outcome (6).

In a recent meta-analysis study (7), the recanalization rate with IV fibrinolytic therapy was shown to be approximately twice the spontaneous rate, but still less than fifty percent. Intra-arterial fibrinolysis (IA) had a substantially higher rate of recanalization, with reperfusion in approximately two thirds of patients. The IA route offers additional advantages, including the accurate demonstration of the vascular anatomy and the exact knowledge of the timing recanalization is achieved. IA also has disadvantages, including the inherent delay in initiation of fibrinolysis (that typically occurs 50 to 90 minutes later than start of intravenous lytic infusion) and the requirement of tertiary hospitals capable of carrying out acute endovascular therapy.

Newer pharmacological reperfusion strategies are being developed with the goal of extending the therapeutic window of efficacy including: other fibrinolytic agents, combination of lytics and antithrombotics , and externally applied ultrasound (US) to enhance enzymatic fibrinolysis (6,8,9).

Endovascular mechanical therapies offer the highest rate of recanalization with approximately 80% of patients achieving arterial patency. They offer other advantages over IA fibrinolysis including working more quickly, having a lower hemorrhagic risk and being more effective in the treatment of large clot burden (6).

Mechanical interventions include techniques for the removal of thrombi (endovascular thrombectomy) and mechanical disruption devices. Endovascular thrombectomy devices extract occluding thrombi from the target vessel through a catheter. The Merci Retriever is the first reperfusion therapy device labeled

specifically for use in acute ischemic stroke by the FDA. The Merci Retriever is a corkscrew-like device attached to a catheter that is advanced distal to the clot and then pulled back, and gently withdrawn into the guide catheter. Patients who are ineligible for treatment with intravenous tPA or who fail intravenous tPA therapy are candidates for this approach (10).

Mechanical devices, such as angioplasty with or without stent placement, are intended to fragment the thrombi and can also promote stabilization of the atherosclerotic plaque. Repeated passage of a guidewire through a thrombus is another form of mechanical disruption often used during IA fibrinolytic procedures <sup>11</sup>.

Concerning reperfusion injury, no significant difference in the risk of hemorrhagic transformation for recanalized versus non-recanalized patients has been documented (7), suggesting that the severity of the ischemic injury to the blood-brain barrier is an equal or greater determinant of hemorrhagic transformation than whether reperfusion occurs orthograde through the recanalized vessel or retrograde via collateral vessels.

The case related by Sánchez et al.<sup>12</sup>, published in this issue of the RBCI, illustrates that in patients with an angiography related stroke, mechanical thrombolysis or intra-arterial fibrinolysis makes sense and can be accomplished quickly, leading to a rapid restoration of the cerebral blood flow with salvage of ischemic brain and a subsequent good outcome.

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