Advances in Treatment of Acute Ischemic Stroke

Written by Brian Hoyle

Acute ischemic stroke that results from large artery or small vessel atherosclerosis, atrial fibrillation, cervical artery dissection, and unknown etiologies is an important health concern. In the developed world, stroke is the leading cause of disability and the third-most common cause of death, according to Brian van Adel, MD, PhD, McMaster University, Hamilton, Ontario, Canada.

Clinical outcome of stroke is measured with the modified Rankin score. This scale ranks patients in terms of the degree of functional disability, with scores indicating unfavorable or favorable outcomes (ie, return to residence and resumption of some/all aspects of daily living), with higher scores indicating progressively severe degrees of mobility limitation and ultimately death (Table 1).

Ischemia-related damage to the brain depends on the occlusion size, severity of blood flow reduction, duration of ischemia, efficiency of collateral circulation, blood flow restoration, and other factors. Thrombolysis and vessel recanalization are the only neuroprotective treatments supported by clinical evidence [Jauch EC et al. *Stroke*. 2013]. Recanalization can be done pharmaceutically and mechanically. However, vessel restoration does not always result in a good outcome.

Likewise, the outcome of thrombolysis therapy through intravenously administered tissue plasminogen activator (tPA) can vary; it is especially effective when done soon after the ischemic stroke (within 3 hours). Protracted delays before tPA treatment increase the risk of symptomatic intracranial hemorrhage. tPA therapy yields good recanalization in occluded proximal vessels when applied to distal small clots in the intracranial circulation, but the outcome is not as good for other locations, including the basilar artery and internal carotid artery [Bhatia R et al. *Stroke*. 2010].

The time to treatment is crucial. Every minute that a large-vessel ischemic stroke is untreated, 2 million neurons die, and aging is accelerated by over 3 weeks [Saver JL. *Stroke*. 2006]. Current unknowns about acute ischemic stroke treatment through intravenous tPA include the rate of infarct progression, how collateral circulation influences recovery, and the influence of other factors, such as the composition of a clot.

Treatment has advanced from catheter-mediated delivery of tPA for intra-arterial fibrinolysis in the late 1990s to ultrasound coil retrievers and aspiration in the next decade and to the use of various designs of stent retrievers in the past few years.

Table 1. Modified Rankin Score

Outcome: Score	Symptom
Favorable	
0	No symptoms at all
1	No significant disability
2	Slight disability
Unfavorable	
3	Moderate disability
4	Moderately severe disability
5	Severe disability
6	Death

In particular, optimistic results have resulted through the use of newer stent retrievers in the following studies: MR CLEAN [ISRCTN10888758; Fransen PSS et al. *Trials*. 2014], ESCAPE [NCT01778335; Goyal M et al. *New Engl J Med*. 2015], EXTEND-IA [NCT01492725; Campbell BCV et al. *New Engl J Med*. 2015], SWIFT PRIME [NCT01657461; Saver JL et al. *New Engl J Med*. 2015], and REVASCAT [NCT01692379; Jovin TG et al. *New Engl J Med*. 2015]. These trials have spurred the recommended use of mechanical thrombectomy in addition to intravenous tPA to treat acute ischemic stroke with large-artery occlusions within 6 hours of symptom onset. Mechanical thrombectomy should be done as soon as possible.

Current Treatment of Superficial Vein Thrombosis and Cerebral Venous Thrombosis

Written by Emma Hitt Nichols, PhD

Recommendations for treatment of superficial vein thrombosis (SVT) of the legs now include anticoagulation; however, the low quality of evidence to support this recommendation and the uncertainty of cost-effectiveness have resulted in the question: Do patients with SVT require treatment? Hervé Décousus, MD, CHU de Saint-Etienne, Saint Etienne, France, discussed the management of spontaneous acute SVT of the legs.

Several studies have demonstrated that deep vein thrombosis (DVT) and pulmonary embolism (PE) are present in 25% to 29% of patients who present with primary or secondary SVT [Frappé P et al. *J Thromb Haemost*. 2014; Galanaud JP et al. *Thromb Haemost*. 2011; Décousus H et al. *Ann Intern Med*. 2010]. In addition, patients with isolated SVT are at an increased risk of developing a subsequent DVT or PE between 3 and 6 months, with rates of up to 3.1% and 0.9% for DVT and PE, respectively [Décousus H et al. *J Thromb Haemost*. 2015]. Patients with SVT are at risk of SVT