Severa factors determine outcome after an acute ischemic stroke (AIS). These include type of stroke, speed of occlusion, presence of collateral circulation, as well as comorbid medical conditions. Recanalization is important in improving outcome. The results of the large German stroke registry, the MERCI registry, the MULTI-MERCI trial demonstrate a clear correlation of arterial recanalization with improved outcome after AIS.1

The only approved therapy for improving outcome of AIS came from the NINDS intravenous thrombolysis trial in 1995 demonstrating an ARR of 11% to 13% after 3 months in achieving a modified Rankin score (mRS) of $\leq 1$ across all groups of patients with AIS.2 Interestingly, patients treated within 90 minutes did better than those treated after 90 minutes within the 3-hour window. This difference was significant and suggests that earlier treatment is associated with a better outcome. However, when analyzed by stroke severity, the magnitude of the benefit declined with increasing NIHSS scores. Patients with NIHSS scores $>20$ had a $\leq 6\%$ ARR in achieving mRS $<1$ at 90 days. This suggests that patients with large vessel occlusions with a high clot burden, as would be expected with internal carotid artery (ICA), main stem middle cerebral artery (M1), or basilar artery (BA), are less likely to improve with the present accepted and FDA approved intravenous thrombolysis (IV) strategy. Can we do better with intraarterial (IA) thrombolysis or combined IA/IV thrombolysis in these patients with large vessel occlusion?

Class 1B angiographic proof for reperfusion and good outcomes for large vessel occlusion with intraarterial therapy came from the PROACT II trial (prolyse in acute cerebral thromboembolism). There was a significant 15% increased chances of a good outcome, defined as a MRS score of 0 to 2 at 90 days when patients with M1 occlusion were treated with intraarterial prourokinase within a 6-hour time window without increase in mortality, compared to those who did not receive this intervention. This correlated with a 48% greater reflow in treated patients.3 Although the Interventional Management Study (IMS11), a trial that combined IV and IA therapy, was considered a negative trial in terms of the primary outcome, the group treated with combined IV and IA therapy had a better outcome than the placebo-treated patients of the NINDS trial and if secondary outcome measures were considered (Barthel Index and the Global Scale), a statistically better outcome was seen with combined therapy compared to the IV-treated group of the NINDS trial. Of the 74 patients who underwent an angiogram after receiving IV rt-PA (0.6 mg/kg with a 15% bolus), the majority achieved a TIMI grade 2 to 3 flow after additional IA thrombolysis (43% treated within 3 hours and 13% between 3 to 4 hours). Of the 28 patients with ICA occlusion, 56% achieved a TIMI reflow of 2 to 3 which correlated with the outcome of a mRS $\leq 1$. Of the remaining patients with ICA occlusions who had a TIMI of 0 to 1, only 12% had a similar good outcome. Two important conclusions can be drawn from the IMS-2 trial. First, recanalization was achieved only after rescue IA therapy in the majority of patients. Second, those patients treated with the combined therapy within 3 hours had a significantly better outcome than those treated within the 3- to 4-hour window.4

Several retrospective studies have suggested that IA thrombolysis is superior to IV thrombolysis in patients with ICA, BA, or M1 occlusions associated with the dense MCA sign. In a large retrospective study comparing IA versus IV treatment in M1 occlusion demonstrating the dense MCA sign matched for age and stroke severity, IA treatment was associated with a significantly better outcome despite the delayed time to treatment with IA treatment.5 Similar smaller studies of ICA or BA occlusion suggest the superiority of IA thrombolysis over IV thrombolysis. Furthermore, even though data on reopening major arterial occlusion after AIS with devices is mainly registry based, the results are comparable to those reported in the PROACT study without a significant increase in symptomatic hemorrhage. Whether we
can do better with the combined or operator-based selected device or thrombolysis remains a question that will hopefully be answered by the 2 ongoing trials, Interventional Management Study -3 (IMS 3) and MR Rescue.

Given all the presently available data, if we follow the guidelines of intravenous thrombolysis within the first 3 hours after stroke onset for all AIS, we have a less than 30% chance of reopening large arteries (ICA, MCAM1, or BA, especially proximal BA occlusions) with IV t-PA versus a 60% to 70% chance with IA thrombolysis.

Although it is not entirely clear whether reopening blood vessels equals reperfusion, all the present data from metaanalysis of thrombolytic trials, retrospective large database analysis, and case series suggest that it does. Why else would we have resolution of perfusion deficits and shrinkage/stabilization hyperintensity on diffusion-weighted imaging after successful establishment of reflow?6

Maybe it is time to reassess our options when we consider the mode of thrombolysis for AIS presenting within the 3-hour window. The paradigm may be as follows. AIS, Perform CT/CTA/±Perfusion CT or MRI/MRA/±Diffusion-Perfusion MRI. If patients have a major large vessel occlusion (ICA, M1, or BA) and considerable mismatch, consider IA treatment. If significant delays in starting IA are anticipated, IV thrombolysis can be initiated followed by IA treatment if patient fails to recanalize. For all other cases consider IV thrombolysis.

Disclosures

None.

References


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