Intravenous thrombolysis is effective for the treatment of acute stroke up to 4.5 hours after symptom onset

Several randomised trials have shown that intravenous thrombolysis (IVT) with recombinant tissue plasminogen activator (rt-PA, Actilyse®) improves stroke outcome when given within 4.5 hours after onset of symptoms [1]. IVT is effective in all stroke patients treated within 4.5 hours, except those with minor (NIHSS score ≤4) or very severe stroke (NIHSS score >25), in whom the effect is equivocal [2].

Intraarterial thrombolysis is effective

Three randomised trials have shown that intraarterial thrombolysis (IAT) is effective for the treatment of acute occlusion of the main stem (M1) or main branches (M2) of the middle cerebral artery (MCA). Two trials used pro-urokinase and one urokinase, and there was a benefit for treatment up to 6 hours after symptom onset [3]. However, in PROACT II, the largest randomised trial of endovascular treatment, IAT was effective only in strokes with NIHSS scores of 11 or greater. This indicates that the ideal patients for IAT are likely to be those with severe strokes. It has also been shown that patients with NIHSS scores ≥12 will almost always show occlusion of a large vessel such as the carotid T, M1 or M2 segments of the MCA, or of the basilar artery [4]. Hence these are ideal candidates for IAT. Several open series have also shown that IAT can be performed safely after failed IVT with persistent vessel occlusion. This approach is called “bridging” and is useful in networks where hospitals with primary stroke unit teams cooperate with a hospital with a comprehensive stroke unit. Today there are not only pharmacological means of reopening an occluded vessel that caused a stroke. There is a whole armamentarium of mechanical means to restore blood flow, such as thrombus aspiration, retriever devices, and retrievable and permanent stenting [5].

Acute stroke: which intervention for which patient?1

There are independent predictors of outcome after acute stroke

As stroke has many aetiologies and many different clinical presentations, there are also many independent predictors of outcome, some of which can be modified and some not. Nonmodifiable risk factors are the patient’s age, the location of the occluded vessel, the clinical severity of the neurological deficit as assessed by the NIHSS or another scale, collaterals as seen on arteriography, or diabetes; modifiable risk factors are time to treatment, recanalisation or treatment-related haemorrhagic complications. The goal of stroke treatment is therefore to act fast, to recanalise efficiently and to use safe procedures that do not cause bleedings as treatment complications.

Imaging can replace the clock for decisions to treat in some patients

Several studies have shown that a combination of diffusion- and perfusion-weighted MR imaging or perfusion CT can depict viable tissue, called penumbra, that can be salvaged if reperfused [6]. The persistence of viable tissue depends on blood flow over collaterals and is highly variable among individual patients. In general, there are better collateral channels with occlusions of larger arteries than with peripheral occlusions, and penumbral tissue persists longer in occlusions of larger vessels causing more severe strokes compared to peripheral branch occlusions causing less severe deficits. Selected patients with severe stroke will show viable tissue even later than 6 hours after stroke onset and can potentially be treated by mechanical recanalisation to reperfuse the penumbral tissue.

Is IAT more effective than IVT?

To date, no randomised trial has answered this question. A nonrandomised comparison of patients with hyperdense MCA signs on CT, which is a sign of MCA main stem occlusion, showed better outcomes after IAT than after IVT. A similar study showed better outcomes after bridging than after IVT. For patients with basilar artery occlusion IAT achieves higher recanalisation rates than IVT, but to date

1 Lecture at the symposium for the official inauguration of the Neurocenter of Southern Switzerland, May 6, 2010.
better clinical results have not been demonstrated. At present, data from nonrandomised studies indicate that stroke patients with peripheral branch occlusions probably benefit more from IVT and patients with large vessel occlusions most from IAT or bridging IVT plus IAT.

Key words: acute stroke; treatment; intravenous thrombolysis; intraarterial thrombolysis

References