Bridging Therapy in Acute Ischemic Stroke
Are We Ready for a New Standard of Care?

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See related article, pages 993–997.

Sixteen years after the results of The National Institute of Neurological Disorders and Stroke rtPA Stroke Study, intravenous alteplase (IV tissue plasminogen activator [tPA]) is still the unique recommended therapy for patients with acute ischemic stroke.1 Since 1995, no other acute stroke therapy has replaced this gold standard, but is IV tPA really a silver bullet? For sure, acute stroke therapy needs improvement in critical issues such as recanalization. Inability to achieve stable recanalization with IV tPA correlates with poor clinical outcome; in this context, can we be satisfied with recanalization rates with IV tPA of 9% for internal carotid arteries or even 35% for middle cerebral arteries (MCA)?2–7 With the combination of IV and intra-arterial thrombolysis (ie, the “bridging therapy”), there is an opportunity to combine the advantages of 2 strategies: the rapidity of administration of the IV route and the arterial recanalization monitoring with additional thrombectomy of the endovascular approach.

In this issue of Stroke, Rubiera et al report significantly higher recanalization rates with the “bridging therapy” compared with an IV tPA nonresponder control group (45.2% versus 18.1%, P=0.002). This increase in recanalization rates translated into more patients functionally independent at 3 months (OR, 3.75; 95% CI, 1.62 to 8.67). Previous studies have shown increased recanalization rates with the “bridging” approach but failed to show a significant clinical benefit at 3 months (OR, 1.23; 95% CI, 0.80 to 1.90 for Intentional Management of Stroke [IMS] and OR, 1.67; 95% CI, 0.86 to 3.23, for REcanalisation using Combined intravenous Alteplase and Neurointerventional ALgorithm for acute Ischemic Stroke [RECANALISE]).8,9 In IMS II and RECANALISE studies, the bridging therapy was not considered only for IV tPA nonresponder patients but for all patients with ischemic stroke 3 hours and documented arterial occlusion. With the Rubiera et al study, the benefit of the “bridging therapy” seems to increase when the target population is limited to IV tPA nonresponder patients. However, the reverse side of the medal is the safety. Albeit nonsignificant, a higher morbidity–mortality was associated with the “bridging therapy” in the Rubiera et al study (OR, 1.49; 95% CI, 0.70 to 3.16 for death and OR, 2.14; 95% CI, 0.58 to 7.83 for symptomatic intracranial hemorrhage). Is this observation due to the fact that IV tPA nonresponder patients are more severe or are we facing a narrow benefit–risk ratio? Like in carotid endarterectomy trials that showed clinical benefit at the expense of a maximum of 6% periprocedural risk at 30 days, trials will show that the clinical benefit of IV–intra-arterial procedures will be obtained at the expense of a procedure-related complication rate (eg, 10% symptomatic intracranial hemorrhagic risk) and limited to patients experiencing MCA or carotid occlusions. In IMS II and RECANALISE studies, mortality and intracranial bleeding were similar between “bridging therapy” and control groups with 10% symptomatic intracranial hemorrhage and 17% of deaths. Nonetheless, these findings illustrate that safety is the main limit of the “bridging approach.” This safety profile may not appear favorable compared with the European Cooperative Acute Stroke Study (ECASS) III trial and Safe Implementation of Thrombolysis in Stroke–International Stroke Thrombolysis Registry (SITS-ISTR) with rates of intracranial hemorrhage of approximately 2.5%.10,11 Should we remember that these trials did not include patients based on documented large artery occlusions and that studies that focused on IV tPA-treated patients with proximal MCA and persistent occlusion reported mortality rates as high as 42%?12 These elements underline the need to evaluate therapeutic approaches in the subset of different ischemic stroke populations (eg, limited to patients with large vessel occlusions of the anterior circulation). In this perspective, a remake of the Prolyse in Acute Cerebral Thromboembolism (PROACT) II study13 limited to patients with MCA occlusions and a control group including the gold standard (ie, IV tPA) is relevant. This is supported by a meta-analysis on mechanical endovascular therapy showing that patients with a favorable outcome are those with an isolated MCA occlusion and treated in association with thrombolysis.14 Pending the results of ongoing randomized trials such as IMS III, there is evidence to support “bridging therapy” as a therapeutic alternative in patients with acute ischemic stroke and documented intracranial artery occlusion such as the MCA. Last but not least, it is not clear to what extend the “bridging therapy” is a model of provision of care applicable to every stroke unit with accessible endovascular therapists and facilities 24 hours/day. We definitely need more than one string to our bow …

Disclosures

None.
References


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