38th Mihara Award Memorial Lecture

The randomized study of endovascular therapy with versus without intravenous tissue plasminogen activator in acute stroke with ICA and M1 occlusion (SKIP study)

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Introduction

Endovascular therapy (EVT) has been adopted as an evidence-based treatment for acute ischemic stroke in addition to intravenous thrombolysis with recombinant tissue-type plasminogen activator (IVT) (1). The major mechanisms for proving the effectiveness of EVT are a high reperfusion rate and a reduction in the time from onset to reperfusion. Whether IVT preceding EVT is useful remains unclear. As EVT can achieve a high rate of recanalization, IVT ahead of EVT might increase the potential risk of bleeding complications without increasing the reperfusion rate.

Several nonrandomized studies have reported on acute ischemic stroke patients treated using direct EVT. Most reports have shown that IVT preceding EVT enhanced survival and successful recanalization without carrying any bleeding risk. In contrast, other reports have shown that direct

EVT was associated with lower rates of intracranial hemorrhage (ICH) and mortality. No established data have been accumulated from randomized, controlled trials of direct EVT in patients within 4.5 h from onset. We hypothesized that direct EVT is as effective as and also safer than conventional bridging therapy for acute ischemic stroke patients with large vessel occlusion (LVO) within 4.5 h from onset. We thus planned a multicenter trial to test this hypothesis.

Methods

The randomized study of EVT with versus without Intravenous recombinant tissue-type Plasminogen activator in acute StroKe with ICA and M1 occlusion (SKIP Study) is an investigator-initiated, multicenter, prospective, randomized, open-treatment, blinded-endpoint clinical trial comparing direct EVT and bridging therapy with IVT and EVT. This trial is registered with the UMIN clinical trial (ID: 000021488).

Patient population

Acute ischemic stroke patients with occlusion of the internal cerebral artery or horizontal part of the middle cerebral artery represent the target population in the SKIP study. The occluded vessel is evaluated by magnetic resonance angiography (MRA) or computed tomographic angiography (CTA).

Randomization

Eligible patients were randomized 1:1 to undergo either direct EVT (direct EVT group) or bridging

therapy with IVT and EVT (bridging therapy group).

Treatment or intervention

Patients randomized to the direct EVT group receive EVT without IVT. EVT can be performed using several devices). Patients randomized to the bridging therapy group receive IVT preceding EVT. Intravenous recombinant tissue plasminogen activator (rt-PA) is administered at 0.6 mg/kg body weight up to a maximum of 60 mg, 10% as bolus, and 90% as continuous infusion over 1 h according to the Japanese guidelines. EVT has to be initiated as soon as possible, within 90 min from hospital admission.

Primary and secondary outcomes

The primary efficacy endpoint is that direct EVT would be noninferior to bridging therapy with respect to the rate of favorable outcome as defined by mRS 0-2 at 90 days after stroke onset. The safety endpoint is any ICH.