The stroke care revolution

After the release of findings from highly anticipated trials at this year's International Stroke Conference in Nashville (TN, USA; Feb 10–13), attendees could not hide their enthusiasm. The excitement seems justified: endovascular therapy can improve functional outcomes in selected patients with stroke and might revolutionise standard care.

Intravenous alteplase administered within a 3 h or 4·5 h window after symptom onset is the only approved treatment for acute ischaemic stroke in the USA and Europe, respectively. Alteplase treatment increases the likelihood of a good functional outcome at 3 months, irrespective of the patient's age or stroke severity, and despite the associated increased risk of intracranial haemorrhage. However, many patients have contraindications (eg, coagulation problems or history of brain haemorrhage) that preclude its use. Furthermore, good clinical outcome depends on recanalisation of the occluded vessels, which can be poor in many patients receiving alteplase. Hence, there is clearly an urgent need for other therapeutic options.

Alteplase was first approved for the treatment of myocardial infarction in the 1980s, but it was not until the 1990s that the drug was approved for ischaemic stroke. Cardiologists also pioneered the use of thrombectomy devices, and several well designed, multicentre, randomised controlled trials (RCTs) are now proving the benefits of these approaches in patients with stroke.

The Multicenter Randomized Clinical Trial of Endovascular Treatment of Acute Ischemic Stroke in the Netherlands (MR CLEAN) was—in the words of Werner Hacke—"the first step in the right direction". In this trial, intra-arterial therapy plus usual care was safe and more effective than usual care (absolute difference of 13·5 percentage points in the rate of functional independence, assessed by modified Rankin scale [mRS] scores at 90 days) in patients with a proximal arterial occlusion of the anterior circulation confirmed by angiographic imaging. The MR CLEAN results have been confirmed by those of other studies presented in Nashville and two of these trials have been published: Endovascular Treatment for Small Core and Anterior Circulation Proximal Occlusion with Emphasis on Minimizing CT to Recanalization Times (ESCAPE) and Extending the Time for Thrombolysis in Emergency Neurological Deficits—Intra-Arterial (EXTEND-IA).

An interim analysis after the release of the MR CLEAN results at the 2014 World Stroke Congress led to the early termination of ESCAPE. This trial compared standard care with standard care plus endovascular treatment by use of thrombectomy devices in patients with proximal vessel occlusion, a small infarct core, and moderate-to-good collateral circulation, assessed by neurovascular imaging. Again, the rate of functional independence, also measured by mRS scores at 90 days, was better in the intervention group (53·0% *vs* 29·3% in the control group, p<0·001).

Similar to ESCAPE, EXTEND-IA was stopped early because of efficacy. The trial compared intravenous alteplase plus thrombectomy by use of a stent retriever with intravenous alteplase alone in patients with proximal cerebral artery occlusion. These patients had to have salvageable tissue according to standardised CT perfusion imaging. Neurological improvement at 3 days and reperfusion (coprimary outcomes) were both better for those who underwent endovascular therapy than for patients receiving alteplase only. Most secondary and tertiary outcomes in these three trials (including functional independence assessed by mRS at 90 days in EXTEND-IA) also favoured the endovascular interventions. Results from other trials (eg, SWIFT-PRIME, REVASCAT, and THERAPY) have not been published yet, but will further help to inform patient selection and methods for intra-arterial thrombectomy. However, in most settings, these interventions are too complex and expensive to be delivered, and future research must clarify their benefits and cost-effectiveness. For endovascular therapy to become standard care in routine practice, pragmatic trials will be needed, which could be completed more quickly if regulatory authorities would mandate the evaluation of new technologies (neuroimaging and stents) exclusively within the context of RCTs.

The important findings from MR CLEAN, ESCAPE, and EXTEND-IA are generalisable only to stroke centres that have advanced imaging facilities and endovascular therapy expertise, and are able to provide swift assessment of patients and mobilisation of interventional staff. The path to implementation of endovascular therapy as standard care has started, but will not be accomplished soon without the integration of clinical research into routine clinical practice; that's the revolution this field urgently needs. ■ *The Lancet Neurology*

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For the **MR CLEAN results** see *N Engl J Med* 2015; **372:** 11–20

For the **ESCAPE results** see *N Engl J Med* 2015; published online Feb 11. DOI:10.1056/NEJMoa1414905

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