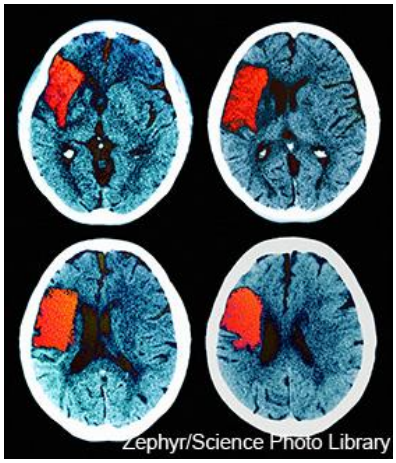
Intra-arterial treatment for acute ischaemic stroke

A Dutch randomised controlled trial found that people with acute ischaemic stroke who received mechanical thrombectomy, intra-arterial thrombolysis, or both, plus usual care were more likely to be independent and free from disability at 3 months than people who received usual care alone.



Overview: A stroke occurs when the blood supply to part of the brain is cut off, either by a blood clot (ischaemic stroke) or when a weakened blood vessel supplying the brain bursts (haemorrhagic stroke; NHS Choices 2014).

People with acute ischaemic stroke can be treated with intravenous thrombolysis, such as alteplase, which dissolves the blood clot and restores the flow of blood to the brain. However, alteplase is effective only if used very soon after onset of stroke (Emberson et al. 2014) and has limited efficacy in opening blockages of the major arteries in the brain (Bhatia et al. 2010).

Treatments that are delivered directly to the area of the blood clot are an alternative approach. Intra-arterial treatments can be broadly divided into those that apply thrombolytic agents to the affected area to dissolve the clot (intra-arterial thrombolysis) and those that break up or remove the clot using mechanical devices (mechanical thrombectomy).

Data from randomised trials indicate no advantage for intra-arterial thrombolysis over intravenous thrombolysis (IMS-3 trial and Synthesis trial). The efficacy of mechanical clot removal for treating acute ischaemic stroke is also not clear, and the procedure is associated with risks of serious complications (NICE 2013).

Current advice: The NICE guideline on stroke recommends thrombolysis with alteplase in people with acute ischaemic stroke. The technology appraisal on alteplase adds that treatment should be started as early as possible within 4.5 hours of onset of stroke symptoms. NICE does not have guidance on intra-arterial thrombolysis.

The NICE interventional procedure guidance on mechanical clot retrieval for treating acute ischaemic stroke states that clot removal can be used in patients with acute ischaemic stroke for whom thrombolysis is unsuitable or has failed. The procedure should be used with special arrangements for clinical governance, consent and audit or research. Selection of patients for mechanical clot removal should be done by clinicians experienced in the use of thrombolysis for stroke. The procedure should

be carried out in specialist centres by experienced interventional neuroradiologists with appropriate facilities and support.

The NICE pathway on stroke brings together all related NICE guidance and associated products on the condition in a set of interactive topic-based diagrams.

New evidence: An open-label randomised controlled trial at 16 centres in the Netherlands compared intra-arterial treatment plus usual care with usual care alone in acute ischaemic stroke. The Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands (MR CLEAN) by Berkhemer et al. 2015 recruited people with acute ischaemic stroke caused by a proximal occlusion in the anterior circulation of the brain.

People randomised to the intra-arterial treatment group received mechanical thrombectomy, intra-arterial thrombolysis or both. Usual care could include intravenous administration of alteplase. The primary outcome was degree of disability or dependence at 90 days, measured by the modified Rankin scale (7-point scale, with a score of 2 or less indicating functional independence).

A total of 233 (46.6%) people were randomly assigned to intra-arterial treatment plus usual care (intervention group) and 267 (53.4%) to usual care alone (control group). Intra-arterial treatment was performed in 196 (84.1%) people in the intervention group: 195 had mechanical thrombectomy and 1 had intra-arterial thrombolysis. Nearly all participants received intravenous alteplase (87.1% of the intervention group and 90.6% of the control group).

At 90 days, people in the intervention group were more likely to have a lower score on the modified Rankin scale than people in the control group (adjusted odds ratio [OR]=1.67, 95% confidence interval [CI] 1.21 to 2.30). A third (32.6%) of patients in the intra-arterial treatment group were functionally independent (modified Rankin score 0 to 2) compared with 19.1% of the control group (adjusted OR=2.16, 95% CI 1.39 to 3.38).

The proportion of people who had serious adverse events during the 90-day follow-up was similar in the intervention group (47.2%) and the control group (42.3%, p=0.31). No significant difference was seen in mortality at 7, 30 or 90 days of follow-up.

Strengths of this study include that intracranial arterial occlusion was confirmed with imaging. Limitations include that the control group was larger than the intervention group, and participants were not blinded to treatment allocation.

Commentary by Phil White, Professor of Neurointerventional and Diagnostic Neuroradiology, Newcastle University and Honorary Consultant Neurointerventionist, Newcastle upon Tyne NHS Foundation Trust:

“The MR CLEAN trial has had a major impact worldwide on stroke research and clinical practice. Since this study was first reported, 5 ongoing trials of intra-arterial treatment reviewed their data and stopped early because a pre-specified end point had been reached (ESCAPE, EXTEND-IA, REVASCAT, SWIFT-PRIME and THRACE trials). These recent thrombectomy data are compelling, generalisable and robust. Although trials that stop early do tend to overestimate effect size, this caveat does not apply to MR CLEAN.

“What is most exciting and striking regarding thrombectomy is the consistency among trials in reporting a large clinical benefit despite different protocols, populations and imaging criteria for selection of participants. To improve outcome by 1 point on the modified Rankin scale, just 3 to 4 patients need to be treated within 6 hours, compared with more than 10 patients treated within 4.5 hours for intravenous thrombolysis (Brunström and Carlberg 2015).

“Typically in large-vessel occlusive stroke, less than 40% of patients treated with intravenous thrombolysis alone will be alive and independent at 90 days. However, with appropriate tissue-based imaging selection, intravenous thrombolysis combined with early thrombectomy increases the proportion of people alive and independent at 90 days to 61–71% (EXTEND-IA and SWIFT-PRIME).

Furthermore, the major advantage for thrombectomy is in reducing the proportion of people with severe disability after stroke, so the health economic advantage is likely to be greater still.

“Selecting participants on the basis of imaging findings was key to the positive results of MR CLEAN. Replicating these results in the NHS would mean at the very least obtaining vascular imaging (CT angiography) and systematically recording any changes on CT head imaging (via Alberta Stroke Program Early CT [ASPECTS] score) in all acute stroke patients potentially eligible for intra-arterial treatment. In addition, NHS stroke care services would need to be reconfigured for patients with large-vessel occlusive stroke to facilitate rapid access to thrombectomy that can be delivered within published standards of care.

“Although the findings of this study are positive, some uncertainties remain around how best to implement intra-arterial treatment – for example, whether to treat large-vessel occlusive stroke with thrombectomy on basis of CT or CT angiography findings alone, or whether to refine selection further with brain perfusion imaging.”

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