

M. Goyal, A. M. Demchuk, B. K. Menon, M. Eesa, J. L. Rempel, J. Thornton, *et al.* Randomized assessment of rapid endovascular treatment of ischemic stroke. The ESCAPE Trial Investigators. *N Engl J Med.* 2015 Feb 11. [Epub ahead of print]

Ischaemic stroke is a devastating condition with a high burden of neurologic disability and death. As a systemic treatment, intravenous alteplase has been shown to be better than conservative care.^[1,2] Among patients with a proximal vessel occlusion in the anterior circulation, 60–80% of patients die within 90 days after stroke onset or do not regain functional independence despite alteplase treatment.^[3,4] However the Prolyse in Acute Cerebral Thromboembolism (PROACT) II study was the first positive trial of endovascular treatment involving patients with angiographically visualized occlusion of the middle cerebral artery.^[5] Recent studies have shown the superiority of retrievable stents over the previous generation of thrombectomy devices.^[6,7] The recently reported Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke (MR CLEAN) have shown clinical benefit with endovascular treatment.^[4] The Endovascular Treatment for Small Core and Anterior Circulation Proximal Occlusion with Emphasis on Minimizing CT to Recanalization Times (ESCAPE) trial was designed to test whether patients with acute ischemic stroke, who were selected on the basis of results of computed tomography (CT) and CT angiography (CTA), would benefit from rapid endovascular treatment involving contemporary endovascular techniques.^[8] Here they aimed to evaluate rapid endovascular treatment in addition to standard care in patients with acute ischaemic stroke with a small infarct core, a proximal intracranial arterial occlusion, and moderate-to-good collateral circulation.

Participants were randomly assigned to receive standard care (control group) or standard care plus endovascular treatment with the use of available thrombectomy devices (intervention group). Randomization was performed with the use of a real-time, dynamic, Internet-based, randomized minimization procedure (minimal sufficient balance method) to achieve distribution balance with regard to age, sex, baseline National Institutes of Health Stroke Scale (NIHSS) score (range, 0–42, with higher scores indicating greater stroke severity), site of arterial occlusion, baseline.

Alberta Stroke Program Early Computed Tomography Score (ASPECTS), and status with respect to intravenous alteplase treatment. The ASPECTS scale is a 10-point scoring system to quantify early ischaemic changes in the middle-cerebral-artery territory, with a score of 10 indicating normal and 1 point subtracted for each abnormal region. The Participants in the intervention group underwent rapid endovascular treatment with recommended retrievable stents. During thrombus retrieval, suction through a balloon guide catheter in the relevant internal carotid artery was also recommended. The control group received the current standard of care as described in the Canadian or local guidelines for the management of acute stroke.^[9,10] Participants in both groups received intravenous alteplase within 4.5 hours after the onset of stroke symptoms. Patients with a proximal intracranial occlusion in the anterior circulation were included up to 12 hours after symptom onset. Patients with a large infarct core or poor collateral circulation on CT and CTA were excluded. The primary outcome was the score on the modified Rankin scale [range, 0 (no symptoms) to 6 (death)] at 90 days.^[11] *Secondary outcomes* included early recanalisation and reperfusion, intracranial haemorrhage, angiographic complications, neurologic disability at 90 days, and death.

The trial was stopped early because of efficacy. At 22 centres worldwide, 316 participants were enrolled, of whom 238 received intravenous alteplase (120 in the intervention group and 118 in the control group). In the intervention group, the median time from study CT of the head to first reperfusion was 84 minutes. The rate of functional independence (90-day modified Rankin

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score of 0–2) was increased with the intervention (53.0%, vs. 29.3% in the control group; $P < 0.001$). The primary outcome favored the intervention (common odds ratio, 2.6; 95% confidence interval, 1.7–3.8; $P < 0.001$), and the intervention was associated with reduced mortality (10.4%, vs. 19.0% in the control group; $P = 0.04$). Symptomatic intracerebral haemorrhage occurred in 3.6% of participants in intervention group and 2.7% of participants in control group ($P = 0.75$). Secondary clinical and imaging end points favoured the intervention group. The rate of patients with a score on the Barthel Index of 95–100 at 90 days was 57.7% in the intervention group versus 33.6% in the control group, the rate of patients with a 90-day NIHSS score of 0–2 was 51.6% versus 23.1%, and the median 90-day score on the EuroQoL Group 5-Dimension Self-Report Questionnaire (EQ-5D) visual-analogue scale (range, 0–100, with higher scores indicating better quality of life) was 80 versus 65.

Authors concluded that the ESCAPE trial, in which fast and efficient workflow, innovative imaging, and effective thrombectomy devices were used, provides evidence of the benefit of endovascular treatment in patients with moderate to severe ischaemic stroke. Patients with acute ischemic stroke with a proximal vessel occlusion, a small infarct core, and moderate-to-good collateral circulation, rapid endovascular treatment improved functional outcomes and reduced mortality. This trial confirms the benefit of endovascular treatment reported recently in the MR CLEAN trial.^[4] The trial attempted to deliver rapid endovascular therapy to patients who were selected for inclusion on the basis of imaging. It also achieved shorter interval times than those seen in past trials, with a median time from study non contrast CT to first reperfusion of 84 minutes. MR CLEAN and the ESCAPE trial showed benefit and low complication rates with endo-vascular treatment that was performed predominantly with retrievable stents. Factors that distinguish the ESCAPE trial from MR CLEAN and prior trials of endovascular treatment for stroke include the use of imaging to exclude participants with a large infarct core and poor collateral circulation, a shorter interval from symptom onset to treatment initiation, a low rate of general anaesthesia (9% in the ESCAPE trial vs. 38% in MR CLEAN), and a higher rate of successful reperfusion. These differences may account for the higher proportions of good outcomes and the larger effect size observed in the ESCAPE trial. However this trial has some limitations. First, they purposefully did not involve screening logs (which tend to yield poor-quality data) and cannot provide an estimate of how many patients were ineligible on the basis of imaging criteria. Second, a majority of participants were enrolled at selected endovascular centres that are capable of implementing efficient workflow and imaging processes. Although the time targets used in this trial may appear daunting, the

history of intervention for acute coronary syndromes suggests that such efficiency in workflow is widely attainable.^[12,13]

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