# The ESCAPE Trial: Rapid Endovascular Treatment Leads to Better Outcomes

Written by Muriel Cunningham

Michael D. Hill, MD, and Mayank Goyal, MD, University of Calgary, Calgary, Alberta, Canada, jointly presented the results of the ESCAPE trial [Goyal M et al. *N Engl J Med*. 2015], a phase 3, multicenter, prospective, randomized, open-label, controlled trial with a blinded outcome evaluation. The study was conducted at 22 centers in Canada, the United States, South Korea, the United Kingdom, and Ireland. Patients were randomized in a 1:1 ratio to modern endovascular treatment plus guideline-based care (intervention group) or guideline-based care alone (control).

Eligible patients had to have acute ischemic stroke (National Institutes of Health Stroke Scale [NIHSS] > 5) within a 12-hour window and good premorbid functional status. There was no upper age limit for participants in the study. Results from the patient's imaging were required to show a small core, proximal intracranial artery occlusion, and moderate-to-good collateral circulation using computed tomography (CT) or multiphase CT angiography. The use of magnetic resonance imaging was discouraged.

The study focused on rapid endovascular treatment, with a target time of 60 minutes from head CT (first slice) to groin puncture and 90 minutes from head CT to the first reperfusion, to enable fast imaging and interpretation. Intravenous tissue plasminogen activator (tPA) was administered to appropriate patients according to standard of care. The investigators were encouraged to use retrievable stents and balloon guide catheters and to avoid general anesthesia. The primary outcome was the modified Rankin scale (mRS) score 90 days post-randomization. Safety end points were also measured.

The ESCAPE trial steering committee stopped recruitment in October 2014 after the presentation of the MR CLEAN trial results [Berkhemer OA et al. *N Engl J Med*. 2015]. A planned interim analysis was completed early, and ESCAPE was discontinued by the Data Safety Monitoring Board in November 2014 because the prespecified efficacy boundary had been crossed.

A total of 316 patients were enrolled, 165 in the intervention group and 150 in the control group; 1 patient was excluded due to informed consent issues. Baseline characteristics were similar in the 2 groups: median age close to 71 years, > 50% women, median NIHSS scores around 16, and approximately one quarter with occlusion of the internal carotid artery. In the intervention group, the median time from CT to groin puncture was 51 minutes, from CT to first reperfusion was 84 minutes, and from stroke onset to first reperfusion was 241 minutes. Around 75% of each group received intravenous tPA.

Efficacy and safety end points are presented in Table 1. Benefits in mortality, morbidity, and quality of

Table 1. ESCAPE Efficacy and Safety Outcomes

| Outcome | Intervention (n = 165) | Control (n = 150) | cOR or RR (95% CI) | Adjusted cOR or RR (95% CI) |
|---|---|---|---|---|
| mRS primary outcome (shift analysis) | – | – | 2.6 (1.7 to 3.8) | 3.1 (2.0 to 4.7) |
| mRS 0 to 2 at 90 d, % | 53.0 | 29.3 | 1.8 (1.4 to 2.4) | 1.7 (1.3 to 2.2) |
| NIHSS at 24 h, median (IQR) | 6 (3-14) | 13 (6-18) | | |
| EQ-VAS at 90 d, median (IQR) | 80 (60-90) | 65 (50-80) | | |
| **Serious Adverse Events, %** | **Intervention (n = 165)** | **Control (n = 150)** | **RR (95% CI)** | **Adjusted RR (95% CI)** |
| Death | 10.4 | 19.0 | 0.5 (0.3 to 1.0) | 0.5 (0.3 to 0.8) |
| Large MCA/malignant MCA stroke | 4.8 | 10.7 | 0.5 (0.2 to 1.0) | 0.3 (0.1 to 0.7) |
| sICH | 3.6 | 2.7 | 1.4 (0.4 to 4.7) | 1.2 (0.3 to 4.6) |
| Access site hematoma | 1.8 | 0 | – | – |
| MCA perforation | 0.6 | 0 | – | – |

cOR, combined odds ratio; EQ-VAS, EuroQoL Group 5-Dimension Self-Report Questionnaire visual analog scale; IQR, interquartile range; MCA, middle cerebral artery; mRS, modified Rankin scale; NIHSS, National Institutes of Health Stroke Scale ; RR, rate ratio; sICH, symptomatic intracerebral hemorrhage.

Source: Goyal M et al. *N Engl J Med*. 2015.

life were observed when the intervention arm was compared with the control arm.

Additional subgroup analyses favored intervention across all groups including patients over the age of 80 years. The investigators concluded that endovascular thrombectomy is a safe intervention, reducing mortality and disability when patients are carefully selected using imaging, when treatment is administered very quickly, and when safe, effective technology, such as retrievable stents, is employed.

## CADISS Revealed Low Recurrent Stroke Rate in Patients With Cervical Artery Dissection

Written by Alla Zarifyan

Hugh S. Markus, BM Bch, University of Cambridge, Cambridge, United Kingdom, presented the first results of the Cervical Arterial Dissection in Stroke Study (CADISS) trial [ISRCTN44555237]. The CADISS trial demonstrated that the recurrent stroke rate due to cervical artery dissection appears to be low, with no significant difference in outcome by using antiplatelet vs anticoagulant treatment for future stroke prevention. Investigators also determined that the number of patients needed to show a difference between treatment arms was high and could be challenging to obtain.

Carotid and vertebral dissection is an important cause of stroke in young and middle-aged patients, accounting for up to 25% of cases [Beletsky V et al. *Stroke*. 2003; Touzé E et al. *Neurology*. 2003]. It carries an associated risk of recurrent stroke, although the reported numbers vary widely, depending on the study reviewed. Physicians usually prescribe either anticoagulation or antiplatelet agents to prevent recurrent strokes; however, data from randomized controlled trials showing the superiority of one treatment over another are currently lacking, with some nonrandomized data providing inconclusive results [Kennedy F et al. *Neurology*. 2012].

CADISS was a randomized, open-label trial, with blinded adjudication of end points [Markus HS et al. *Int J Stroke*. 2007]. The primary aim was to determine whether antiplatelet vs anticoagulation treatment was more effective at preventing stroke in patients with acute cervical dissection. The secondary aim was to measure the frequency of recurrent stroke in this population. Initially, 250 patients were recruited in order to establish whether there would be a sufficient number of clinical end points to determine a treatment effect, and if an adequate number of patients can be feasibly recruited. The primary end point was ipsilateral stroke or death at 3 months. Eligible patients had to have symptoms of ipsilateral stroke or transient ischemic attack, or ipsilateral Horner syndrome, neck pain, or headache within 7 days of recruitment.

Out of 250 patients, 126 were randomized to antiplatelets and 124 to anticoagulants. End points included 4 ipsilateral strokes (all in patients presenting with stroke; 3 in antiplatelet group and 1 in anticoagulant group) and 1 subarachnoid hemorrhage (in anticoagulant group). No deaths were reported. The overall stroke rate was strikingly low at 1.6% (2.1% in those presenting with stroke or transient ischemic attack). Given the low number of events, the difference between treatment arms was not significant (Table 1).

A predefined per-protocol analysis was also performed after excluding patients whose diagnosis of dissection could not be confirmed by reviewing their imaging data. Overall, 53 patients were excluded. The per-protocol analysis included 197 patients. There were 3 per-protocol end point events (defined as stroke, major bleeding, or death) among 101 patients in the antiplatelet group and 2 among 96 patients in the anticoagulant group (Table 2), with insignificant difference between treatment arms.

Table 1. Association Between Treatment and Risk of End Point Event in ITT Population

| | Anticoagulants, n (%) (n = 124) | Antiplatelets, n (%) (n = 126) | OR | 95% CI | *P* Value |
|---|---|---|---|---|---|
| Ipsilateral stroke or death | 1 (0.8) | 3 (2.4) | 0.335 | 0.006 to 4.233 | .63 |
| Any stroke, death, or major bleeding | 2 (4.0) | 3 (3.2) | 0.673 | 0.055 to 5.983 | 1.00 |
| Any stroke | 1 (0.8) | 3 (2.4) | 0.335 | 0.006 to 4.233 | .63 |
| Ipsilateral stroke, TIA, or death | 5 (4.0) | 4 (3.2) | 1.280 | 0.268 to 6.614 | .98 |
| Any stroke, TIA, or death | 5 (4.0) | 5 (4.0) | 1.017 | 0.228 to 4.540 | 1.00 |

ITT, intent to treat; TIA, transient ischemic attack.

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