



ARTICLE OF THE MONTH

Thrombectomy for Stroke at 6 to 16 Hours with Selection by Perfusion Imaging

Albers GW, Marks MP, Kemp S, Christensen S, Tsai JP, Ortega-Gutierrez S, McTaggart RA, Torbey MT, Kim-Tenser M, Leslie-Mazwi T, Sarraj A, Kasner SE, Ansari SA, Yeatts SD, Hamilton S, Mlynash M, Heit JJ, Zaharchuk G, Kim S, Carrozzella J, Palesch YY, Demchuk AM, Bammer R, Lavori PW, Broderick JP, Lansberg MG; DEFUSE 3 Investigators. *N Engl J Med*. 2018 Feb 22;378(8):708-718. doi: 10.1056/NEJMoa1713973. Epub 2018 Jan 24. PMID29364767

Welcome to the May 2018 installment of the SNACC Article of the Month! In the selected article, Albers et al look at the effectiveness of endovascular thrombectomy for ischemic stroke between 6 and 16 hours from onset of symptoms in a group of patients with internal carotid artery or proximal segment middle cerebral artery occlusion.

This month's expert commentator is Dr. Caroline Cook from the University Hospital in Southampton, United Kingdom. Dr. Cook is a neuroanesthesiologist who provides anesthetic care for adult and pediatric complex cranial and spinal surgery and interventional neuroradiology. She is currently the Neuroanesthesia Lead in Southampton.

We continue to encourage our readers to join us on the [Twitter](#) feed or on [Facebook](#).

~ Nina Schloemerkerper, MD, Adrian Pichurko, MD, and Oana Maties, MD

Commentary

Caroline Cook, MBBS, BSc, MRCS, FRCA

Intra-arterial thrombectomy (IAT) for acute ischemic stroke is a developing time-critical therapy for the management of proximal occlusion of the internal carotid or first segment of the middle cerebral arteries. Endovascular therapies can improve outcomes in terms of functional independence when compared to conventional medical therapy with number needed to treat (NNT) = 4.¹ It has been demonstrated that the absolute chance of being functionally independent at 90 days after thrombectomy diminishes by 3.4% with each hour's delay to starting the procedure.² Current recommendations are that eligible patients should be treated within six hours of symptom onset. A number of recently published studies have started to look at specific subgroups of patients with ischemic, but not yet infarcted brain tissue (penumbra), who may benefit from thrombectomy during an extended time window of up to 24 hours.³ The volume of the penumbra was assessed

by RAPID (iSchemaView), an operator-independent system for processing perfusion- and diffusion-weighted MRI images.

Albers *et al*, on behalf of the DEFUSE 3 Investigator group, conducted a multicenter, randomized, open-label trial with blinded outcome assessment of patients who had a thrombectomy six to sixteen hours after they were last known to be well and who had remaining ischemic brain tissue that had not yet infarcted. Patients were eligible for inclusion if they had an initial infarct volume of <70 ml, a ratio of volume of ischemic tissue to initial infarct volume of 1.8 on perfusion imaging and an absolute volume of potentially reversible ischemia (penumbra) of 15ml or more. Randomization was to endovascular therapy (which took place within 90 minutes of qualifying image) plus standard medical therapy or standard medical therapy alone. Primary outcome was modified Rankin scale (mRS) at 90 days (range = 0 to 6, with higher scores denoting greater disability). A secondary efficacy outcome was functional independence (mRS 0-2) at 90 days.

The trial was terminated early for efficacy, having randomized just 182 patients. Endovascular therapy plus medical therapy demonstrated improved outcomes at 90 days compared to standard medical therapy alone.

A favorable distribution of functional outcomes at 90 days was demonstrated with a higher percentage of patients being functionally independent (defined by mRS 0-2) in the endovascular and standard treatment group than those with standard therapy alone (45% vs. 17%, $P<0.001$). 90-day mortality was 14% in the endovascular plus medical therapy group compared to 26% in the medical therapy group alone ($P=0.05$). No statistically significant difference was seen between the groups in terms of primary safety outcomes or serious adverse events. Imaging outcomes showed no difference in lesion growth at 24 hours.

Reperfusion of more than 90% at 24 hours was more common in the endovascular and medical therapy group than the standard treatment group (79% vs 18%, $P <0.001$). Similarly, complete recanalization of primary arterial occlusive lesion at 24 hours on CTA or MRA was higher in the endovascular group (78% vs 18%, $P<0.001$).

One limitation of the study was that the power to assess response to therapy in subgroups was limited owing to a lower than anticipated number of patients being enrolled. The low rate of favorable outcomes in the control group in comparison to other six-hour trials in the literature may be related to the small proportion of patients in this trial who presented in time to receive intravenous thrombolysis with tPA. Finally, general anesthesia was discouraged and it is yet to be determined what effect this may have on outcomes.

In summary, this study has shown positive outcomes for patients with ischemic stroke and specific imaging parameters up to sixteen hours after symptom onset. These extended time windows will have implications for future service design and delivery.

References:

1. Berkhemer OA, Fransen PSS, Beumer D, et al. for the MR CLEAN Investigators. A Randomized Trial of Intraarterial Treatment for Acute Ischemic Stroke. *N Engl J Med* 2015; 372: 11-20.
2. Saver JL, Goyal M, van der Lugt A, et al. Time to Treatment With Endovascular Thrombectomy and Outcomes From Ischemic Stroke: A Meta-analysis. *JAMA*. 2016;316(12):1279-89.
3. Nogueira RG, Jadhav AP, Haussen DC et al. for the DAWN Trial Investigators. Thrombectomy 6 to 24 Hours after Stroke with a Mismatch between Deficit and Infarct. *N Engl J Med* 2018;378:11-21.