Interventional Management of Acute Stroke

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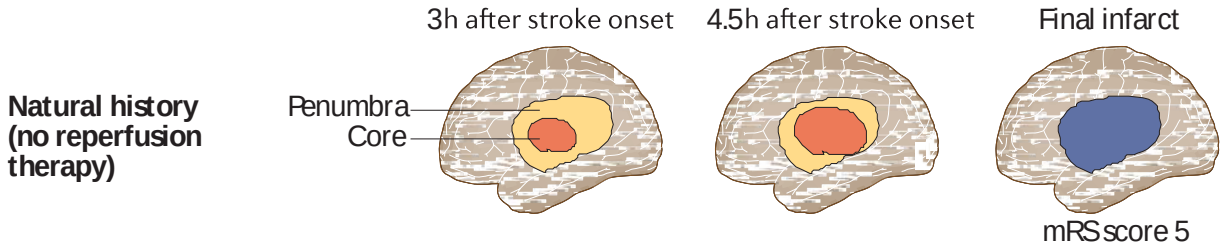
Endovascular Clot Retrieval for Acute Ischaemic Stroke

Background:
Acute ischaemic stroke results usually from occlusion of an intracranial vessel causing nutritional deficiency to the area of the brain supplied by the blood vessel. Within the region of ischaemic brain are regions of 'ischaemic penumbra', which is viable brain tissue at risk of infarction without timely reperfusion, in addition to regions of already infarcted brain tissue term the 'ischaemic core'. Without timely reperfusion there is progressive demise of the viable ischaemic penumbra resulting in enlargement of the ischaemic core leading to functional disability or death (figure). Reperfusion strategies target the salvage of the ischaemic penumbra.

Figure. The concept of ischaemic penumbra and core with infarct progression in the absence of reperfusion. From J Baron 2018 (1).



Intravenous thrombolysis
Intravenous thrombolysis with alteplase is effective at reducing disability compared to standard medical treatment when given within 4.5 hours of stroke symptom onset (2). However the effect diminishes exponentially with time with most benefit seen within the first 60 to 90 minutes of symptom onset time. However intravenous alteplase has limited efficacy in patients with proximal intracranial occlusion, with recanalization achieved in approximately 30% of patients with proximal middle cerebral artery occlusion and 10% or less in those with terminal internal carotid artery or basilar artery occlusion (3). Patients with large proximal intracranial occlusion generally have a high risk (~70-80%) of permanent severe disability or death in the absence of recanalization.

Endovascular clot retrieval
In late 2014 and 2015, the results of 5 multi-centre multi-national randomised controlled trials demonstrating efficacy of endovascular clot retrieval (ECR) in treatment of anterior circulation large vessel occlusion were published in quick succession in the New England Journal of Medicine (4-8). Endovascular clot retrieval resulted in successful removal of large intracranial clots in between 60 to 80% of patients and functional independence at 90 days was achieved in approximately 50% of patients in otherwise devastating stroke (3). In these studies most patients had to have the angiogram commenced within 6 hours of symptom onset thus limiting the therapeutic window.

The limitation of the 6-hour time window is obvious, particularly for patients who live remote to a primary intervention stroke centre. In many rural hospitals in Australia and New Zealand it may not be possible to have groin puncture started within 6 hours of symptom onset time following unavoidable delays in inter-hospital transfer. However experience from the Australia-New Zealand multicentre EXTEND-IA study, which was only trial to select patients for ECR on basis of favourable perfusion pattern, suggest that treatment for patients beyond 6 hours may be possible provided viable brain issue (penumbra) can be demonstrated (4). Furthermore, the individual patient meta-analysis also suggests the therapeutic window extends beyond the 6-hour time window (9).

Recently two randomised controlled trials in DEFUSE 3 and DAWN examined the effect of ECR on outcome in the so-called extended time window. Both these trials utilised advanced imaging in the selection of patients for treatment. In the DAWN trial ECR was performed in patients with a small ischaemic core with a severe clinical deficit and an intracranial arterial occlusion between 6 and 24 hours of last known well time. In DAWN 49% of treated patients achieved functional independence compared with 13% of patients receiving best medical treatment which is stroke unit care (10). The DEFUSE 3 trial utilised perfusion imaging similar to the criteria set out in EXTEND-IA and performed ECR in patients 6-16 hours from last known well time. DEFUSE 3 also demonstrated overwhelming efficacy in favour of thrombectomy patients with 45% functional independence rate compared with 17% in the medical treatment arm (11). There is a shift in the selection paradigm from a time-based approach to a 'tissue' based approach utilising advanced imaging or a radiological time clock. Furthermore, there is suggestion that treatment of patients beyond 24-hours may be possible (12) and may well be topic of future randomised trials.

Areas of uncertainty

General anaesthesia versus conscious sedation

An area of controversy is the choice of anaesthetic approach during ECR. Procedures may be performed more smoothly under general anaesthesia due to lack of patient agitation and may reduce procedural time. However associated delays in setting up general anaesthesia and the hypotension associated with anaesthetic induction may exacerbate ischaemic injury. To date 3 single centre randomised controlled trials (AnStroke, GOLIATH and SIESTA) (13-15) have been reported. All these trials comprised of relatively small sample size (AnStroke n=90, GOLIATH n=128, SIESTA n=150) each with different primary end points. In terms of 90-day functional outcomes only SIESTA reported a difference in rates of functional independence favouring the general anaesthesia group while no difference in independent outcome was reported in GOLIATH and AnStroke (13-15). More recently the individual patient meta-analysis from the HERMES collaboration (which consisted of patients from recently published ECR trial) comprised of 797 patients (236 had general anaesthesia) reported reduced odds of favourable functional outcome with general anaesthesia when compared with conscious sedation (16). However there was no standardisation of intra-operative haemodynamic control or anaesthetic agents used across these studies,- factors which may account for the conflicting results reported to date. Further multi-centre studies with standardised intraoperative anaesthetic management are needed to address this question.

Treatment of patients without pre-existing functional disability

The initial positive trials of ECR and the two 'extended' time window trials required patients to have strict pre-stroke functional independence with modified Rankin Scale score of 0-1. However, this would exclude patients who have mild to moderate baseline disability from previous stroke or other medical issues but otherwise are living at home independently. For example, a patient with mild chronic right leg weakness from a previous stroke, who had ceased driving since a stroke, who required a walking frame but was living at home independently would have been ineligible for inclusion into trials. In the recently published EXTEND-IA TNK study which demonstrated superiority of low dose tenecteplase (0.25mg/kg) than alteplase at achieve recanalization of large intracranial clot before clot retrieval had a broader inclusion criterion of baseline modified Rankin Scale score 0-3 (17). This study demonstrated 57% of treated patients had returned to their baseline functional capacity at 90 days. Selection criteria for treatment varies from centre to centre but the experience from the EXTEND-IA TNK study suggest that patients with pre-existing mild to moderate disability with an intracranial occlusion should be considered for clot retrieval.

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