ECR for CVA

When to suck it up...

Nepean WTET summary 26/5/20

Background and Rationale

- Endovascular clot retrieval (ECR) is playing an increasingly important role in the treatment of ischaemic stroke (or cerebrovascular accident, CVA). It can be delivered as a stand-alone therapy (in certain instances) or as an adjunct to thrombolytic therapies. It is becoming a standard of care and regional networks are being established to ensure 24/7 cover are available to patients irrespective of geographical location.

- Those who theoretically have most to gain are those with a large (salvageable) ischaemic penumbra. Even ability to deliver early ECR however should not compromise thrombolysis where indicated, as no studies (to my knowledge) have looked at comparing early ECR alone versus thrombolysis where thrombolysis is not contraindicated.

- Modified Rankin score (mRS) 0-6 provides a useful grading system for assessing degree of in/dependence (0 = no disability, 1-2 = mild, 3 = moderate, 4-5 = severe, 6 = death).

Advantages and Disadvantages

- Advantages
  - Reduces disability further in many who meet (and receive) thrombolysis
  - Few absolute contraindications; true anaphylaxis to contrast (even difficult access can often be circumnavigated)
  - Offers a therapy to those where thrombolysis is contraindicated (post major surgery) or would be futile (e.g. embolism of calcified material from aortic cross clamp of calcified aorta, patients with subacute bacterial endocarditis, SBE)
  - Does not increase poor functional survival (high dependence)

- Disadvantages
  - Potentially needs transfer to specialised center, +/- procedural general anaesthesia
  - Recognised complications: Failure (due to technical difficulties versus failure to restore flow despite therapy versus restoration of flow without clinical benefit), ischaemic stroke in new vascular territory, vasospasm; but probably not increased in intracerebral haemorrhage (ICHg – was reported in some studies, maybe more marked in posterior circulation ECR). Access site injury (haematoma, pseudoaneurysm, dissection)
  - Changing BP targets; AHA/ASA 2018 guideline recommend slightly different BP targets for ECR (<180/105 for 24h) compared to fibrinolytic therapy alone (<185/110 for 24h)

Evidence

- MR CLEAN NEJM 2015
  - MC RCT (Netherlands) n=500. Proximal intracranial arterial occlusion in anterior circulation (mostly ICA/M1/M2) <6h onset of symptoms; usual care alone vs usual care plus ECR
  - 89% of all patients received thrombolysis with alteplase, in the treatment arm 84.1% underwent intraarterial therapy (mostly retrievable stents) & 12.9% had carotid stenting also
  - Improved mRS (13.5% more people had mRS 0-2) and functional independence at 90d in the intervention group, without significant difference in mortality or occurrence of symptomatic ICHg

- Other studies (EXTEND-IA, ESCAPE, SWIFT-PRIME, REVASCAT) looked at up to 12h safe and effective at reducing disability
**HERMES meta-analysis LANCET 2016**
- 5 RCTs (MR CLEAN, ESCAPE, EXTENDIA, SWIFT PRIME & REVASCAT) n=1287
- Endovascular thrombectomy of proximal anterior circulation ischaemic CVA within 12h of symptom onset, significantly reduced disability by at 90d (P<0.0001); NNT 2.6 to reduce mRS by at least one level
- Benefit held even if /=/>80y/o or delayed >300mins and irrespective of thrombolysis status. In fact not significant benefit in younger (<50y/o), low stroke severity score (NIHSS=/<10), more distal (M2) disease

**DEFUSE 3 NEJM 2018**
- MC RCT (US) n=182 (terminated early for efficacy & results of DAWN) ICA or proximal MCA (M1) occlusion and infarct size <70ml and ratio of ischaemic -to- infarcted tissue =/>1.8 on perfusion CT/MRI presenting 6-16h after onset of symptoms; standard care +/-thrombectomy
- More favourable mRS with functional independence at 90d in 45% vs 17% (P<0.001) in thrombectomy (intervention) arm

**DAWN NEJM 2018**
- MC RCT (Bayesian adaptive-enrichment design) US/Ca/EU/Au n=206 (terminated at interim analysis -for efficacy). Presenting 6-24h after last known to be well, large MCA CVA (>1/3 MCA territory) with small-medium volume infarct core and minimal pre-existing disability (mRS 0-1) either too late or persistent occlusion after alteplase. Standard care +/-thrombectomy
- Improved functional independence at 90d (49% vs 13%) with minimal increase in infarct volume (1ml vs 13ml from baseline) in the thrombectomy arm
- More symptomatic ICHg at 24h in intervention group (6% vs 3%). Very select group with potentially most to gain (average 8.3ml infarct vol). Industry funded (Stryker Neurovascular)

**Beyond 24h?**
- Retropective studies looking at patients meeting DAWN criteria but last seen well >24h suggest this may be safe, feasible and effective

**What about the posterior circulation?**
- A number of retrospective observational studies have shown ECR is safe, feasible and effective, with high rates of near-complete and complete reperfusion and increased favourable outcomes when compared to natural history or thrombolysis alone
- Meta-analysis Kumar et al (2016); recanalisation of basilar artery occlusion (intravenous thrombolysis +/- ECR) reduces mortality two fold and risk of death or dependency 1.5 fold
- THRACE (2016) included superior 1/3 basilar artery CVA, but only 2 patients with this location included as usual care in France is for endovascular approach for these strokes
- BEST trial (2020) MC RCT <6h vertebrobasilar occlusion (China) n=131 terminated early due to poor recruitment and high crossover; in the intention to treat analysis no difference in favourable mRS (0-3 unusually) at 90d; but improved mRS when comparing groups receiving intervention when compared to those with standard care (?patient selection – equipoise lost). Higher prevalence of symptomatic ICHg with intervention

**Summary (my practice)**
- Where patients meet the specific criteria there is excellent evidence for ECR (with stent retriever) in anterior circulation CVA (ICA, MCA M1/M2 divisions) 0-6h and 6-24h for ICA and MCA M1 divisions where salvageable ischaemic penumbra exists on imaging amongst other criteria (specifics of which depends on time at presentation)
- The evidence beyond 24h and for posterior infarcts (basilar occlusion in particular) is less strong but still exists. Equipoise is probably lost with regards to randomising posterior circulation infarcts
- The goal posts for feasibility and benefit of ECR are ever changing (some emerging studies looking at those with larger core sizes) – I image and refer urgently (whilst providing optimal supportive care to include thrombolysis where indicated), unless there is a clear clinical reason not to (short life expectancy or severe pre-existing disability, with new large established stroke – excluded from many of aforementioned studies) on a patient-by-patient basis