The DAWN Trial: An Update on Thrombectomy for Stroke
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Take Home Points

- Multiple studies have shown benefit to endovascular intervention in a highly selected cohort of stroke patients.
- The DAWN study found benefit to endovascular intervention in patients with ICA or MCA stroke and a last known well time of 6 to 24 hours prior to presentation.
- The average duration of symptoms was 13 hours.
- This was an industry funded study using a single device.
- It is unclear how this will impact EMS triage and transport to stroke centers.

- In 1996, NIMS was published and stroke care was altered forever. The harms and benefits of alteplase were widely discussed. In 2014, the discussion shifted again and centered around endovascular therapy for stroke.
- In 2014, the MR CLEAN trial was published and followed by multiple articles over the next 12 months.
    - The MR CLEAN trial showed that endovascular therapy improved outcome for patients with acute ischemic stroke. This was important because three studies were published in 2013 in the New England Journal of Medicine which did not show improvement in outcome with endovascular therapy.
  - After the MR CLEAN publication, REVASCAT, EXTEND-IA, SWIFT PRIME closed their books early and showed results with improved outcome. This was a defining moment for stroke neurology and identified endovascular intervention as an option in addition to tPA.
  - Part of the reason they were able to demonstrate benefit is that they selected the right patients. They used CT and MR perfusion imaging to select the best patients for endovascular therapy. They looked for patients with a small core infarct and a larger penumbra. Tissue in the penumbra may be salvaged. They also had a short time to groin puncture. In MR CLEAN, the study was supported by the government which led to good enrollment.
  - There were some limitations to these studies. With the exception of MR CLEAN, all of the other trials were stopped early which likely overestimated benefit. They used a very narrow group of patients as candidates. At some centers, only 1-2 patients a month were enrolled.
- When the NIMS study was published, it led to the creation of stroke centers and ambulances bypassed hospitals to go to stroke centers. What has been the impact of these endovascular studies on overall care of strokes? Now that we can show that endovascular therapy works, every hospital with the capability wants to be a comprehensive stroke center because they will catch these patients. This impacts how EMS triages patients and where they go for care. However, it may be difficult to justify maintaining an interventional team if only 1-2 of these procedures are performed every month. We may see indication creep.
This study used either diffusion weighted imaging or CT perfusion to assess patients with delayed presentation to determine who would be eligible for intervention.

This addresses the problem of wake-up strokes. Guidelines currently recommend a consideration of endovascular therapy for patients with anterior large vessel obstruction within 6 hours of their last seen normal time.

Now that we can determine the presence of viable tissue, can we extend the time period even farther?

This study looked at patients 6 to 24 hours out. The trial was stopped early as they found benefit in the treatment arm over the control arm. This trial looked at patients with ICA and MCA stroke only. The patients had to have a mismatch that was predefined as to volume.

They did find a benefit.

On average, patients enrolled in the study were 13 hours after the last seen normal time.

There are some limitations to the study.

- It was industry funded and only used the Trevo device. Many of the authors are on their payroll.
- The authors used the utility-weighted modified Rankin scale instead of the traditional modified Rankin scale. The utility-weighted scale gives more weight to good outcomes than bad outcomes. This may skew the results toward the intervention and makes it difficult to compare results from this study to others.
- The bottom-line: the DAWN group found that using the endovascular intervention resulted in better outcomes up to 24 hours after symptom onset. This is a shift in the paradigm that time=brain to a perspective that patients may still have salvageable brain tissue a long time after symptom onset.

Still, in these studies, the earlier we get to these patients, the better they do.

This study was in large vessel strokes.

- Should we be doing diffusion weighted imaging and CT angiograms in every stroke patient before considering treatment? This would be unreasonable. We need to be smart about this. Look at the patient's function and goals to determine if it makes sense to do advanced imaging. Marcolini would not do DWI or CT perfusion on every case. We have to be careful of indication creep.

- We need to be smart regarding administration of tPA as well. Giving alteplase to patients later on in their disease course has increased risk. We know that giving it earlier decreases the risk of bleed.

- If you suspect a large vessel stroke, should you obtain the perfusion study more rapidly to facilitate intervention? If the patient presents with clinical signs of a large vessel occlusion anterior stroke, Marcolini has her team activated and they often receive a CT and CTA prior to transport for intervention. The CT perfusion or DWI studies are performed in patients where they are unsure if there is a large ischemic penumbra with a small infarct. The imaging modalities need to be tailored to the patient in front of you.

- It is important for us to know the area of distribution in considering eligibility of intervention. For those at smaller hospitals, you need to be careful in determining which patients are eligible for intervention and need transfer to a center for additional procedures.

- Does this change how we triage patients in the EMS setting? This raises questions that have yet to be answered but are under investigation. Where should EMS bring these patients? If EMS is closer to a hospital without endovascular capability, should they stop there for tPA or divert to a comprehensive stroke center? This is an issue in rural areas. How can EMS differentiate between a large vessel occlusion and all other strokes encountered? New stroke scales are in development to help EMS in this process.

- Should we still be giving systemic alteplase? In cardiology, they don't give systemic alteplase if they are close to a center where they can receive PCI. If they are more than 90 minutes away, they are given alteplase and transported for PCI. Is this where stroke management is heading? There are studies in progress examining this question. Is it better to give endovascular therapy with tPA or go directly to a comprehensive stroke center?