Endovascular Therapy for Acute Ischemic Stroke:
Is it "Time" to Change Current Practice?

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Clinical Scenario:
You are working a shift at an ED which is part of a larger network when a patient presents with signs of a stroke. Last known normal time was approximately five hours ago. On your exam, there are no apparent life threats or other acute pathology. Imaging reveals findings consistent with your exam with a large vessel occlusion in an area amenable to endovascular therapy. After reviewing the imaging and discussing the patient, the stroke neurologist recommends transfer to a higher level of care so urgent endovascular intervention can be performed. The patient's family members ask what this new treatment entails, the risks associated, and how much it will benefit their family member as the receiving facility is a long distance from their home. What can you tell the family based on current evidence?

Background
1. Endovascular Thrombectomy for Acute Ischemic Stroke: A Meta-analysis. Jetan H. Badhiwala, MD; Farshad Nassiri, MD; Waleed Alhazzani, MD; et. al. JAMA. 2015 Nov 3;314(17):1832-43.

Discussion
2. Randomized assessment of rapid endovascular treatment of ischemic stroke. Goyal M, Demchuk AM, Menon BK, et al. N Engl J Med. 2015 Mar 12;372(11):1019-30.

3. Endovascular therapy for ischemic stroke with perfusion-imaging selection. Campbell BC, Mitchell PJ, Kleinig TJ, et al. N Engl J Med. 2015 Mar 12;372(11):1009-18.

4. A randomized trial of intraarterial treatment for acute ischemic stroke. Berkhemer OA, Fransen PS, Beumer D, et al. N Engl J Med. 2015 Jan 1;372(1):11-20.

The continuum of stroke care continues to evolve. Thrombolysis is here to stay for acute ischemic strokes and over the past year, a significant amount of "positive" research has emerged regarding the utility of endovascular intervention for ischemic strokes. The background paper (Badhiwala, et al.) was released in JAMA last November and the authors advocate that a certain population of stroke patients have improved outcomes with endovascular intervention.

Interestingly, this evolution also directly parallels the care of patients who have ACS/STEMI. Initially, these patients were treated with thrombolytics, which became the standard of care. Then, endovascular therapy was introduced- the PCI. This also

eventually became standard of care with a modest mortality/mortality benefit seen in a wide variety of STEMI presentations. The adoption of PCI as standard of care within a treatment window has drastically altered practice patterns and shifted everything from where EMS transports STEMI patients to the establishment of referral centers, etc.

Endovascular studies for acute ischemic strokes initially hit the literature in a significant fashion in 2008. The first RCTs were published in 2013 with overwhelmingly negative results. They demonstrated no benefit to endovascular intervention with markedly poor outcomes.

The literature re-emerged in late 2014/early 2015 with the results of the "MR CLEAN" trial being published. All of these later studies used a second generation device (the one in the video) that was reported to be the "modern" method for thrombectomy (two years after the initial data was released). The MR CLEAN trial was halted early as it appeared to demonstrate remarkably positive results for the endovascular arm. Unfortunately, this led to a downstream "ripple effect" as several other studies were then halted early as well due to the positive findings of MR CLEAN. Two of these, EXTEND-IA and ESCAPE are included in our journal packet. The authors concluded that further research would be unethical due to the above positive findings. They analyzed their data gathered thus far; publishing it shortly after the MR CLEAN results were released. The results of these trials were synthesized into the Badhiwala, et al. meta-analysis with the 5 studies in the 2015 (later) generation all being stopped early for positive results.

The background paper (Badhiwala, et al.) compiles all the above studies and also argues for the positive outcomes associated with endovascular intervention. At first glance, this appears to be a markedly superior intervention, but looking more deeply at the papers, several concerns begin to emerge such as device manufacturer support of studies, highly selective controls/criteria for inclusion that limits it to only a small fraction of stroke patients, outcome heterogeneity between the studies, etc.

Bottom Line: In conclusion, looking at the above, it is concerning to think that we might dramatically alter our stroke care systems to focus on such an intervention. In EXTEND-IA, approximately 1k of the 7.7k patients screened received thrombolytics. That means only 7% of the patients that received the thrombolytics in that study qualified for endovascular intervention. Approximately 5% of patients in the US with acute ischemic strokes qualify for thrombolysis (based on the literature I found), which means 0.35% would qualify for this intervention with a marginal benefit. The cost/benefit ratio is astounding considering the very modest benefit afforded by the intervention. It would be reasonable to conclude that this intervention could offer benefit, but further research is necessary to conclude whether more stroke patients might benefit than the small percentages included in these studies' intervention arms.