[MUSIC PLAYING]

CIARAN POWERS: Good afternoon. My name is Ciarán Powers. I'm an endovascular neurosurgeon and associate professor in the Department of Neurological Surgery at Ohio State University Wexner Medical Center. I'm also the surgical director of our Comprehensive Stroke Center. I'm going to talk to you this afternoon about thrombectomy for large-vessel occlusions or LVO.

We're going to talk about the study supporting the use of thrombectomy large-vessel occlusions, the ones that revolutionized stroke care, and then other studies that expanded the window from within six hours out to up to 24 hours.

So just for financial disclosures, I receive clinical research support from Medtronic, MicroVention and Stryker. Also fellowship support for neuroendovascular fellowship through Medtronic.

The basis for these interventions is going to be endovascular. So we use a biplane fluoro suite. This is the system we have at Ohio State. It's a Siemens system. We have anesthesia present for all our cases. It's actually a hybrid operating room. And so we have anesthesia and essential core beyond that door there for other supplies. Most of the supplies are in the room.

And then this is the platform we do the procedures on with the heads-up display. This is what a stentriever looks like. And this device really revolutionized stroke care beyond intravenous tPA. And it allowed us to safely and effectively remove clots from large vessels, in the head large vessels being internal carotid artery, proximal and middle cerebral artery, proximal anterior cerebral artery, as well as the posterior circulation.

And essentially, it's a nickel titanium alloy woven into a stent. It's a self-expanding stent. There's little markers on there so we can see this during life fluoro. And then it's attached to a wire. The stent does not come off. It's not a deployed stent, but it's a way of capturing the thrombus and pulling it out.

This is a representative example, anterior-posterior view of a patient who is having a left middle cerebral artery occlusion. The tip of the catheter, which actually is extending from the femoral puncture site up into the carotid artery here, kind of is visualized here, and then you see the clot up into the supraclinoid space right up here. Posterior cerebral artery, anterior cerebral artery, and then the middle cerebral artery is absent.

What we do then is go through this large catheter with a smaller catheter, a microcatheter, and get up past the clot and then deploy the stent. And when you do that and do an angiographic run, you can see here our intermediate catheter and the stent deployed in one of the M2 branches. And what it does initially is restore antegrade flow.

And then we wait five minutes for the stent to really grab onto the clot well before pulling out with aspiration through the intermediate catheter and also from the long sheath. And this is what it looks like after we get the clot out.

We grade ourselves, our performance and our reauthorization. We call it TICI score. It's sort of modified from the TINI score for cardiac revascularization. Grade 0 is no perfusion. Grade 1 is perfusion past the initial obstruction but limited. Distal branch filling with little or slow distal perfusion.

2a is perfusion of less than half of the vascular distribution of the occluded artery. So like filling just one of the M2 divisions. 2b is perfusion of half or greater the vascular distribution. So two of the M2 branches. And then 3 is filling of all the distal branches. And for functional outcome, we found that 2b and 3 is really what we're striving for for revascularization.

So studies supporting thrombectomy. And I said for about 30 years, our treatment for patients with stroke, if they presented within the three-hour time limit or up to the extended window a 4 and 1/2 hours was intravenous tPA. And these studies really revolutionized stroke care and make now a very exciting time to be taking care of these patients, because it's important what we can do for them.

MR CLEAN was the first study that came out in *New England Journal* in January 2015. This was a multi-center randomized clinical trial of endovascular treatment for acute ischemic stroke in the Netherlands. It was done single country with very centralized health care.

There were adult patients with no upper age limit and had to have some measurable stroke. So an NIH Stroke Scale of greater than or equal to 2. They all got a head CT scan to make sure that there was no evidence of hemorrhage and then documented large-vessel occlusion with CT angiography, MR angiography or just catheter angiography.

And then the intervention was intra-arterial thrombectomy within six hours, whether or not they received intravenous tPA, in patients with largest occlusion of the anterior circulation. So ICA, M1, M2, A1 and A2.

The primary outcome with the modified Rankin scale at 90 days, the secondary outcome was a 24-hour, five-day, and seven-day NIH Stroke Scale as well as ADL measured by the Barthel index. Imaging outcomes were with CTA or MRA at 24 hours after the intervention to measure persistence recanalization and then a final infarct volume assessment at about a week out with CT scan.

The study included about 500 participants, mean age of 65. Almost 60% were men, and about 95% had a pre-stroke MRS of 2 or better. So really no significance really. The mean NIH Stroke Scale was 17. 53% were assigned to control and 46% assigned to intervention.

Of those that underwent intervention, of the 195 patients who underwent mechanical thrombectomy, 190 underwent stent retrieval. About 40% had general anesthesia. 12% required concurrent carotid stenting. 10% received into additional intra-arterial tPA. Only one patient underwent intra-arterial tPA alone.

So here, the primary outcome again with a median modified Rankin score at 90 days, and in the top right here you can sort of see with the intervention group on the top and the control group, a real shift in terms of the no symptoms, minor symptoms, some bothersome symptoms but able to work, unable to work, unable to walk, requiring nursing care 24/7, and bed, that the patient in the control group was about-- very few patients did well, whereas a significant number of patients improved with the IA therapy, almost 50% with the thrombectomy as opposed to less than 40%.

And then the second outcomes with the intervention was the control, with a modified Rankin scale. 0 to 2 at 90 days was 12%. Rankin from 0 to 1 at 90 days was 12% intervention, 33 0 to 2 as opposed to 19% in the control group.

Other studies were going on concurrently, including EXTEND IA, which was done in Australia. And this study ended once the MR CLEAN study was published. ESCAPE, which was a study done in Alberta, also ended prematurely before they could reach statistical significance because of MR CLEAN. All studies show a clear benefit with the endovascular therapy group with a mechanical thrombectomy over best medical management.

When you think about this, this is historically what things look like. On the top here, the black diamonds are cardiac reperfusion, and this has been very successful, in high 80s up to 100% reperfusion in the 2000s, whereas in the neuroendovascular around the rates of reperfusion were almost uniformly less than 30%.

And that's sort of thinking why was that these studies that were done early, before 2010, failed to show a benefit. But when you look at 2015, you'll see the success of the mechanical thrombectomy was much higher with the use of stentriever technology.

So that was good for patients up to six hours, and then the next question was, are there patients that would benefit from thrombectomy beyond six hours? And so the one study that we participated in here at Ohio State was the defuse 3 study. This was a thrombectomy for stroke at 6 to 16 hours, based on perfusion imaging.

So the patients had occlusion of a supraclinoid carotid or proximal middle cerebral artery, had a baseline perfusion imaging, had initial infarcts of less than 70 mL, a ratio of the volume of ischemic tissue on perfusion imaging of 1.8 or more. So a large area at risk on a small core infarct. The intervention was intra-arterial thrombectomy, again with a a modified Rankin scale at 90 days.

The rationale for the study was that from defuse 2, which was the study that looked at infarct growth over time, and we know that this is onset of symptoms. And then when the baseline MRI scan was obtained, for patients with known M1 occlusion. And there are some patients who over MRI obtained 11 hours after the last known well, with a confirmed M1 occlusion of really small infarct. So they were able to survive for a long time, even though they had a confirmed M1 occlusion.

And other patients in a very short period of time went on to develop a large infarct. So there is heterogeneity in the collateral flow in the brain. So some patients can tolerate a large-vessel occlusion up to 11 hours, while others have a core infarct early on, and that the perfusion imaging might help us figure out which patients are which. And we can't help these patients with intervention, but we can help these.

So this is an example what the imaging requirements in the defuse 3 were. M1 occlusion here on the CT angiogram. And then the target i profile of a core of less than 70 mL and a mismatch ratio of greater than 1.8. Also one we see a mismatch file of greater than 50 mL. This is again the same thing.

So this study included 182 participants. The median age was 70. 54% were men. Median NIH Stroke Scale was 16, and they were almost totally evenly divided, 90 to control and 92 to thrombectomy.

And this is the modified Rankin scale at 90 days. In terms of the patients that did well, no symptoms were pretty close between the groups. But if you go up to the patients who had a a modified Rankin scale of 2 or better, significantly more, almost 45% of patients in the vascular therapy, whereas just over 30% in the medical therapy.

We did a subset analysis in these patients. One of the questions that we often wonder about is optimal sedation or anesthesia for patients undergoing thrombectomy. A number of retrospective studies, and we confirmed the same thing, have shown that there seems to be a benefit with conscious sedation or even no intravenous sedation for patients undergoing thrombectomy as opposed to patients undergoing general anesthesia.

And in the end, that's what we found, that the patients in the defuse 3, patients that underwent intervention, the ones that had just conscious sedation had a significantly better outcome than the ones that underwent GA. In fact, the ones that underwent GA were really not that much different than the ones that had just medical therapy alone, suggesting that the benefit of thrombectomy is lost when the patients undergo general anesthesia for the procedure.

DAWN was another study that was going on about same time as defuse 3, going up to 24 hours from last known well. The number of groups were broken down based on age and NIH Stroke Scale and infarct size. But again, used perfusion imaging to sort of determine which patients might benefit. And again, they found that the patients who underwent thrombectomy in this extended time window that met perfusion imaging requirements did better.

So in summary, we have shown here that the thrombectomy for large-vessel occlusions, the patients with an LVO benefit from thrombectomy up to 24 hours from last known well, and the window can be determined by functional imaging.

And so the question here then is, can we go beyond 24 hours? And studies are ongoing now looking beyond 24 hours, up to 48 hours, using the functional imaging to say, OK, are there patients that even beyond the time window who might be candidates?

And the idea here being that it's not just time is brain but blood supply is brain and that there are patients that can last longer and that we can avoid them having a big stroke if we intervene beyond an arbitrary time.