

ROBERT BROWN: Greetings. I'm Dr. Robert Brown, Chair of the Division of Stroke and Cerebrovascular Disease at Mayo Clinic. During today's discussion, we'll be talking about stroke and endovascular therapy. I'm joined by my colleagues Dr. Alejandro Rabinstein, David Kallmes, and Giuseppe Lanzino, who are specialists in this area. Welcome. Several recently published studies have demonstrated the effectiveness of endovascular therapy for acute ischemic stroke. Can you provide a general summary of these studies and what we have learned, Dr Rabinstein?

ALEJANDRO RABINSTEIN: That is correct. Last year, we were happy to see the publication of five different randomized controlled trials comparing conventional treatment of acute ischemic stroke which could include intravenous thrombolysis versus acute endovascular therapy primarily through mechanical thrombectomy. You've seen new devices called retrieval stents which are more effective in achieving recanalization or reperfusion of major intracranial vessels. And the results of these five trials were consistently very positive. In essence, they demonstrated that acute endovascular therapy is very effective in improving functional outcomes in patients with major acute ischemic stroke.

The magnitude of the benefit was variable across the trials, but very convincing throughout. To summarize those outcomes, one can say that the proportion of patients that achieved functional independence at 90 days varied between one-third and 71% of the patients treated endovascularly, and that results in a number necessary to treat between three and seven which is, one could say, spectacularly good. And these were compared against patients that could have received intravenous thrombolysis.

Now, one has to take into account that not every stroke patient is a candidate for endovascular therapy. The good candidates are adult patients who have good pre-stroke function, and who present with the same neurological deficits from a proximal intracranial vessel occlusion, and do not have any extensive acute ischemic changes on the head CT scan. Time is also essential. The benefit was greatest when the endovascular treatment could be initiated within six hours of symptom onset. There was some variation across trials in regards to the method of identification of the best patients, or the patients that could be randomized, but overall the substantial benefit achieved by endovascular therapy in these trials has been a game changer in practice.

ROBERT BROWN: Thank you. Dr. Kallmes, Dr Rabinstein did allude to a certain extent to those patients that might be selected for this therapy. From your standpoint, what are the key factors in selecting patients who would be optimal candidates based on the data from the clinical trials?

DAVID KALLMES: He hit a high point, but I would say that, similar to acute MI where time is of the essence, time is brain. And so among the three major factors he talked about, time since onset, degree of neurological deficit, and changes on CT scan, we've always got to focus on time. We are in a non-hurried rush to get the patient to the angiogram table, get the catheter in the artery, and get the clot out. And there have been post-hoc analyzes from these same studies showing that even 15 minutes, even 15 minutes, can yield substantial changes in outcome. So time of onset is key. Get the patient to the angio table as soon as possible.

Secondly, degree of neurological deficit. While some of the trials allowed NIH stroke scale of just two, generally to be a more disabling NIH stroke, eight, nine, or higher, that we want to target for endovascular therapy. And last, we want to look very carefully, look very carefully, at just the plain, old fashioned, 1980s, non-contrast CT scan to look for subtle changes that suggest irreversible injury. We have a scale of zero to ten called the aspect scale, and if the patients score is six or above, that means they have sufficient, probable, salvageable tissue to be a candidate for endovascular therapy. So time, degree of neurological deficit, and findings on old fashioned plain CT scan.

ROBERT BROWN: Thank you. Dr Rabinstein, I would ask you as well. How have these studies changed the early evaluation and management of acute ischemic stroke? In particular, what imaging studies can be used in the emergency room setting to guide the next step in therapy? Dr Kallmes alluded to a CT scan without contrast which has been in place for many, many years. Are there other imaging strategies that you and colleagues have found to be helpful as well?

ALEJANDRO RABINSTEIN: Yes, and some of the trials actually required the use of a CT angiogram to select candidates. Trials before these five positive trials have randomized patients without proof that they had a proximal intracranial vessel occlusion. In these trials, there was a requirement that a CT angiogram be conducted, and it had to prove that there wasn't occlusion in the supraclinoid, most distal portion of the intracranial internal carotid artery, or the proximal segments of the [INAUDIBLE] artery. Furthermore, the same CT angiogram can be used to evaluate, to some degree, the collateral flow which is very important in maintaining viability of the brain tissue when there is a proximal occlusion.

Alternatively, another trial in many centers across the US and other parts of the world use perfusionist scans, either CT perfusion or MRI diffusion perfusion, to determine the mismatch between the core of the infarction that is presumably impossible to salvage versus the total area of hypoperfusion, the difference between these two being the penumbral or salvagable tissue. The big question at this point is whether doing this type of advanced imaging scans is a measure that can improve patient selection enough to account for the extra time that is required for their performance.

ROBERT BROWN: Very good. Thank you. Now, how should a medical center approach care of acute ischemic stroke and, in particular, imaging and endovascular therapies if they're not available, due to great part, rural location of that hospital.

ALEJANDRO RABINSTEIN: Well, I think that that may depend on each center and the logistics of each region, but we have three types of places where acute stroke can be treated. Stroke ready centers, where intravenous thrombolysis can be administered, but the patients then have to be transferred out for additional post-thrombolysis care. Primary stroke centers that can administer intravenous thrombolysis and keep the patients for post-thrombolysis care, and then the comprehensive stroke centers, such as ours, where patients can receive both intravenous thrombolysis, all the subsequent medical treatment, and endovascular stroke therapy.

The current practice is that the patients are triaged to the nearest hospital where they can receive intravenous thrombolysis if the patients are suspected to have an acute ischemic stroke. And they can arrive to the MERCI department so that they can receive intravenous thrombolysis within the accepted window, 4.5 hours from symptom onset. And, from there, the rest of the operation can proceed.

The stroke ready hospitals typically do not have CT angiogram or additional imaging capabilities. In those cases, we rely on the clinical syndrome and decide where the patient should be transferred whether to a primary stroke center or to a comprehensive stroke center. Alternatively, if the patients are in a primary stroke center, we have the option of confirming the presence of a proximal intracranial vessel occlusion amenable to endovascular therapy. In such cases, we proceed with a CT angiogram before deciding on the transfer. If the CT angiogram confirms the presence of a proximal intracranial vessel occlusion, the patient gets transferred to a comprehensive research center. Otherwise, the patient can stay in the primary stroke center.

ROBERT BROWN: Thank you, and it's likely the case too that many hospitals in a rural area now have a connection with a larger medical center via telestroke that can provide an audio or video connection between the tertiary medical center that is a comprehensive stroke center and the rural hospital so as to assist with that acute care.

ALEJANDRO RABINSTEIN: That's very true.

ROBERT BROWN: Dr. Lanzino, from your standpoint, as one of the colleagues who performs this procedure, what are some of the key issues you face in using this procedure for acute ischemic stroke?

GIUSEPPE LANZINO: Well, I think that the two main key issues are related to time to revascularization and selection of patients. Time to revascularization, as Dr Kallmes stressed, is extremely important to go fast. So it's important that there is a full team able to be mobilized within a few minutes, and that often requires a complete culture change to what has been traditionally the care of patients with acute ischemic stroke.

The other factor that has also been alluded before is selection of the correct patients. Despite all advances in imaging, we still are not completely sure about what is the maximum time window to perform these procedures, and we don't want to exclude patients that could potentially benefit from the treatment. But at the same time, we need to utilize resources so that, ideally, only those patients that can benefit from this expensive and resource consuming procedures are effective.

So I think those are two main areas where we can and should continue trying to improve, and as far as time to revascularization, we have improved a lot. But any minimal change that will allow to gain even a few minutes, as Dr. Kallmes mentioned, it's critical to maximize the benefit of the procedure.

ROBERT BROWN: Thank you. Dr. Rabinstein alluded earlier to the remarkable effectiveness of this procedure in acute ischemic stroke. We also recognize that any procedure can have complications associated with it as well, and can you comment? I'll ask both you and Dr. Kallmes to comment. Again, as colleagues who perform this procedure, what are some of the complications that are both alluded to in the clinical trials that were published and experience? What are the things that you most worry about?

GIUSEPPE LANZINO: Well, the main complication is the issue of reperfusion hemorrhage. There is always an established core that is already infarcted in these patients, and the revascularization of that established core in a patient that does often receive thrombolytics has a risk of reperfusion hemorrhage which is, to some extent, a complication that is almost random. And besides trying to control patient's blood pressure within certain limits, there is very little that can be done to prevent that complication. Hemorrhage can also result from vessel perforation during some of these procedures, but that is fairly rare today given advances in imaging and the microcatheter techniques.

The other main neurological complication is distal emboli. As you try to retrieve the embolus, quite often the clot fragments into smaller pieces that can embolize downstream. And despite us trying to prevent that, quite often we do this procedure with the balloon inflated proximally to arrest flow, and try to prevent this complication. There is not infrequently some degree of distal microemboli that obstruct smaller vessels. So I would say those are the two main complications, but luckily with improvement in technology, a better understanding of the disease, and the more experience, these complications are relatively infrequent.

ROBERT Dr Kallmes anything else you--

BROWN:

DAVID I want to re-iterate to take another look at the distal emboli. You can also, unfortunately, as you're pulling that clot, you can send a piece of clot to a new territory. Let's say your primary clot is in the MCA. As you're pulling back, it breaks off and goes to the ACA, INT infarcting territory which can be pretty bad, because now you're infarcting territory that wasn't already at risk. In fact, some of the new trials are looking at INT as a primary outcome, and some of the new devices are being designed with avoiding infarcting new territory as a primary.

ROBERT Thank you. Can you comment as well? In practice, both in the US and, really, throughout the world, now that these procedures are increasingly utilized for acute ischemic stroke, who is performing these procedures in general, both in the US and beyond? What specialty groups are performing these procedures?

GIUSEPPE LANZINO: Well, I think at this stage, the specialty groups involved with the procedures has a lot to do with the local, regional organizations and logistics rather than a planned national effort. That, I think ideally, is what we should be looking at, and there are some required standards to perform these procedures. But we don't have, yet, a well-organized plan to make sure that different specialists performing the procedures are equally prepared to be able to do both safely and effectively, because of, traditionally, intervention radiologies and, more recently, neurosurgeons and neurologists have been involved with these procedures. And there is a lot of experience in the catheterization of the distal intracranial circulation. The vast majority of these procedures are done by these specialty groups, but there are other specialties like the [INAUDIBLE] interventional radiologist and cardiologists that also performing in some areas.

ROBERT Very good. Thank you. Now, as we finish up, I just have one additional question, if I may. And we've talked a lot today about endovascular therapies for acute ischemic stroke, particularly in the carotid distribution, internal carotid artery, middle cerebral artery, anterior cervical artery. Any additional factors that you would like to add regarding posterior circulation, that is, basilar artery thrombosis and our approach in that scenario?

ALEJANDRO RABINSTEIN: Certainly. While true that patients with vertebrobasilar occlusions were not included in the trials that we mentioned before, they have been the vessels that have been historically the most not favorable, but the most often targeted by endovascular therapy simply because medical therapy in those cases often fails. But also, because when medical therapy fails, the prognosis is ominous, so the attempt at opening those blood vessels with catheter based therapies has started. And these trials should not change that. If anything, the advent of better revascularization techniques should make us more aggressive with the management of posterior occlusions by endovascular means.

ROBERT Very good. Thank you. Dr. Kallmas, any additional thoughts?

BROWN:

DAVID KALLMES: Yeah, to compare and contrast anterior versus posterior circulation occlusions, we're much more aggressive in terms of a time window in the posterior circulation than the anterior circulation, going up to 24 hours or more since time of onset is not unusual. And in terms of being aggressive to get the clot out, we will work a little harder to revascularize given the dismal outcomes without revascularization.

ROBERT BROWN: Thank you. Very good. Well, I'd like to thank my colleagues for their insights on this topic, and thank you all for joining us on theheart.org on Medscape.