Gino Mollica: Good afternoon, everyone. Thank you so much for joining us today and welcome to today's webinar. My name's Gino, I'm a Program Manager with the American Heart Association. Today we're going to learn the evolution of current endovascular approaches to acute stroke. Before we get started I'd like to go over a few items so you know how to participate in today's event. The webinar today is being recorded and a link will be sent out within 24 hours after, to review and rewatch the webinar. There are no continuing educations associated with this webinar, but you may access a certificate of completion in your follow up email following today's event. You will have the opportunities to submit questions, please just simply type them into your questions pane of your control panel. You may send in your questions at any time during the presentation, we'll collect these and address them during the question and answer session at today's presentation.

If you experience any technical issues during the presentation today, most can be resolved by refreshing your web browser. If that's not going to allow you to refresh, please refer to the GoTo Webinar technical support email in your registration confirmation today. I will now hand it off to Jeanie Luciano, Senior Get With The Guidelines Program Manager, to introduce our guest.

Jeanie Luciano: Thank you, Gino. Hello, everyone, this is Jeanie Luciano. I'm the Senior Manager for the Get With The Guidelines - Stroke program. May is American Stroke Month and it is absolutely my honor to introduce our first speaker in our webinar series, Dr. Preethi Ramchand. Dr. Ramchand is a Clinical Assistant Professor of Neurosurgery and Medical Director of Neurocritical Care at Main Line Health-Jefferson Neurosurgery. She obtained her undergraduate degree at Princeton University and subsequently attended medical school at the University of Texas, Houston. She completed a residency in neurology and fellowships in both neurocritical care in neuro interventional radiology at the Hospital of the University of Pennsylvania. Her specific clinical interests are the elective and emergent management of cerebral vascular disease in both the critical care and neuro interventional settings, as well as optimization of healthcare delivery to these patients as they move from the emergency room to the endovascular suite, to the ICU and towards recovery. Her community is very fortunate to have her, and we are fortunate that she has joined us today to share her expertise. So Dr. Ramchand, I now hand it over to you.

Preethi: All right. Thank you so much for that introduction and for the opportunity to come and speak with you guys today. This is a topic that is near and dear to me and so I'm always happy to come in and chat about this. So as it said on the slide, we're going to talk today on the evolution of endovascular intervention for acute ischemic stroke. And my goal here is to spend probably the-

Jeanie Luciano: Preethi, are your slides up?

Preethi: Oh, I'm sorry. I thought... Oh, you know what? No, they're not. Hang on one second. Can you see them?

Jeanie Luciano: We can, they're perfect now. Thank you.

Preethi: Okay, sure. Thank you for that. Let me just move this out of the way. Okay, all right. So we're going to talk about the evolution of endovascular intervention. I'm going to spend probably the bulk of the time discussing how we got to where we are in terms of the devices that we used, the development, the advancement of these technologies, and then spend a little bit more time at the end talking about the current clinical landscape.

I don't have any disclosures for this talk. And so just a quick outline, like I said, I'm going to spend the bulk of my time discussing the genesis of how we got to where we are in terms of thrombectomy, the devices that have been trialed and failed and are now part of our arsenal. I'll spend a little bit of time discussing intra-arterial pharmacotherapy, specifically in the way of IA lytics. We'll go through some of the data behind it and the current thoughts in terms of its clinical utility. I'm going to go through the current procedural landscape discussing how we attempt thrombectomy today, and then we'll go through a case example that will hopefully put a lot of these different concepts together.

So before we really get into it, I wanted to start by actually defining what we mean by endovascular intervention. Broadly speaking, there's two big categories of intervention. There's mechanical thrombectomy, which refers to the actual mechanical either removal or disruption of clot embolectomy, so to speak. And then there's intra-arterial pharmacotherapy, and by that we're referring to intra-arterial lytics for the most part, so things like tPA, streptokinase, urokinase, et cetera. The bulk of what we do obviously is more of the former with mechanical thrombectomy, but again there's been a little bit of resurgence of interest in the use of IA lytics and so we'll talk a little bit about that towards the end of this talk.

So I wanted to start by actually putting up what the current guideline recommendations are from the AHA for acute ischemic stroke, specifically as it pertains to endovascular intervention. I apologize for the small print here, but I'll summarize it for you. So it is basically a Class 1 recommendation that patients undergo thrombectomy, they specify with a stent retriever if they meet a number of criteria. So they need to have a good pre-stroke functional quality of life, which we define by the Modified Rankin score. They need to have a stroke in the proximal internal carotid artery or the proximal MCA, so the M1 segment. They need to be adults, 18 or older, a stroke scale of at least 6 or higher, and an ASPECTS score of at least 6 or higher. And treatment needs to be initiated, in other words, groin puncture needs to happen what was initially stipulated as within six hours of last known well, but that window has since been extended to up to 16 hours in light of some publications like the DAWN and the DEFUSE trials.

There is further Class 2b recommendations that certain subsets of patients can also be eligible for mechanical thrombectomy if they have more distal anterior circulation occlusions. So we're talking about M2 or M3 segment occlusions, as well as posterior circulation occlusions, so PCAs, basilar, and vertebral artery occlusions. And of course this is where we are today, but what I'd like to talk about is how we actually got to this point that this is part of our current clinical practice guidelines.

I'm not going to belabor this slide because I know this is a topic that is certainly not unfamiliar to this audience, but I like how it pictorially demonstrates the number of different studies that have come out for thrombectomy. So, as we all know, there were several negative studies that came out in 2013, but subsequent to that there has been a number of large prospective randomized control studies that have shown overwhelming benefit for thrombectomy in patients with large vessel occlusions for acute stroke. But while these guidelines and these current clinical practice recommendations have been relatively recent, within the last decade, the concept of large vessel occlusions, frankly any kind of intracranial intra-arterial occlusion, is not one that is unfamiliar to the neuro interventionalist. You know, really since the advent of these procedures, there has been understanding that everything that we do, whether it's a diagnostic cerebral angiogram, all the way to things that are much more complex like endovascular aneurysm treatment or EVM treatment, every one of these associated with a small, but very real risk of thromboembolism.

And so the concept that we would have to go in and actually physically remove clot from the brain is one that far precedes all of the data that I just presented. And well before the advent of thrombectomy specific devices, things like the stent-triever and the aspiration catheters that we all know, there were a number of techniques that were being trialed to attempt revascularization using existing technologies. And so I'm going to go through what some of these different technologies were and some of the data behind them.

So this was a case series published in the Journal of Neurosurgery in 2001, and it looked at the role of angioplasty for patients with large vessel occlusions that were resistant to intra-arterial lysis, and specifically intra-arterial tPA. It's a relatively small study, about 50 patients enrolled between 1995 and 1999, who underwent IA or intra-arterial tPA, nine of whom had residual distal thromboembolism. And so these nine patients then underwent balloon angioplasty, and just as a quick reminder this is a pictorial schematic of what that looks like. Essentially a balloon is navigated over a wire, into the area of stenosis or occlusion, the balloon is inflated reestablishing circulation in that particular territory. So how do these patients do? Well, five of them had successful recanalization, but unfortunately four had residual distal occlusion, and one had symptomatic intracranial hemorrhage. So it was certainly not an overwhelmingly positive study, but I think it's important to mention as one of the early case series describing how mechanical thrombectomy was being attempted.

Then in 2002 there is a case report that's published in the New England Journal of Medicine, and this describes a 17 year old girl, who has a patent foramen ovale or a PFO and a concomitant DVT, who came in with a very severe brain stem stroke, NIH stroke scale of 24. And the authors describe the successful thrombectomy of this patient using a combination of something called a Neuronet Basket and proximal flow arrest, and I'll talk about each of these things here in just a second.

So just to go through these images, this actually comes directly from the case report itself. So panel C, for some reason, everything is flipped here, but in panel C you see that the vertebral arteries come up, they form the basilar, and then there's an acute cutoff of the basilar in the mid basilar segment, which is of course why she is so clinically symptomatic. She undergoes thrombectomy and, the final image, in panel A you can see successful revascularization with patency of that basilar artery, as well as its distal branches, the PCAs and the SCAs. And then in panel D, that's a picture of that actual Neuronet Basket with clot captured inside of it. So the basket itself, at least to my understanding, is not something that really came to market in a really meaningful way, but the concept of proximal flow arrest is something that is still widely used by interventionalists, and so I'm going to spend just a few minutes discussing what that is.

So this is a diagram that was actually borrowed from a paper that describes the physics of the flow dynamics of how this works, which I'm not really going to get into. But, schematically, what you have here is you have let's say an M1 occlusion. In the absence of proximal flow arrest you'd have a guide sheath positioned somewhere in the proximal circulation, typically in the internal carotid artery, you have a catheter that delivers whatever your thrombectomy setup is, whether it's a stent-triever or an aspiration catheter, into that M1 segment. And like I said, in the absence of proximal flow arrest, you're dealing with continued or persistent normal systolic anterograde blood flow, just normal blood flow that's going to continue throughout the procedure. And some would argue that that is counterproductive to what you're trying to accomplish, which is to try to bring clot out, and potentially that's fighting you with that procedure.

And so with proximal flow arrest they developed catheters that now have a balloon attached as part of the mechanism, the balloon is inflated during the critical portion of the thrombectomy and in that context you essentially create complete stasis of flow. You create a standing column of blood, and there is no further anterograde blood flow for that three to five minutes during the thrombectomy. And there is some data to suggest that that increases the rates of first past success, and also decreases the incidence of further thromboembolism from clot that is potentially not captured during your thrombectomy. So, widely used today and first described now almost 20 years ago in that case report.

All right, then in 2003 there is something called a Technical Note that is published in the Journal of Interventional Neuroradiology, that in many ways really was a seminal piece that laid the foundation for the current application of the stent-triever as it's used today for a thrombectomy. So what is this paper? Why was this so significant? Well, it turns out that the stent-triever, not in its current iteration but in its original model, had actually been created for, developed and approved for use for the treatment of intracranial aneurysms, and specifically it was meant to be an adjunct to coil embolization. So if you look at these schematics, these come directly from this paper itself and it just lays out the structure of the stent-triever. And this is how it's used, so if you have an aneurysm that needs to be coiled and you're concerned about the coil mass staying in place, a stent can be placed at the neck of that aneurysm to keep that coil mass in place. There were a number of stents that had actually been created for that very intent, but these were stents that were deployed intracranial.

So these were things that we would take up into the artery and then detach, and they would stay in the patient forever, along with that coil mass. What made stent retriever so unique was that it came on this pusher wire that allowed you to take it up into the intercranial circulation, leave it there if you needed to, if you needed to detach it you could, but you also had the optionality to bring that stent-triever back out of the body, which was something that was very unique to this particular stent retriever. And so based on that, these authors speculated the following: "... Since the stent is introduced through a microcatheter and is firmly attached to its delivery system, a modification of this design might permit thrombus or foreign body retrieval..." In other words they said, "Why don't we take something that's originally designed and engineered to do this, and maybe with some modification could end up doing something like this?" Which is, of course, one of the mainstays of how a thrombectomy is performed today.

But you can imagine the concept of taking a stent into the intercranial circulation, opening it up, capturing clot and then dragging it out of some very fragile vessels, like the MCAs, with that stent open created some concerns that maybe this could result in interval injury, dissection, spasm, et cetera. And so this was actually trials in a number of animal models first, I think some bovine, sorry, rodent models and some spine models. And then ultimately, in 2008, this was actually the first case series that was published documenting successful thrombectomy with this stent-triever device. So 20 patients in total, a small case series published in Stroke, but 18 of them, so 90%, actually had successful recanalization as defined by the TICI score. And I'll spend a few minutes discussing what the TICI score is in a second. There were two patients who developed symptomatic ICH, and there were four deaths at 90 days, but overall still a very positive study and something that generated quite a bit of excitement.

These are some images from the study itself. So here is a pre thrombectomy angiogram, this is of the left internal carotid artery. Just to orient everybody, this is an AP view looking straight at the patient's head. This is the ICA or the internal carotid coming up, you can see it nicely fills the ACAs, which go medially and then up north, and then laterally it's supposed to go into the MCA but there's a clear cutoff right here at the M1 segment. The stent-triever is then deployed, a run is actually done with the stent-triever deployed that shows complete patency of the distal MCA territory, the stent-triever is then pulled out, and you can see there's quite a bit of clot captured within it. And the subsequent angiogram shows a beautiful TICI 3 reperfusion of the vessel. So, very exciting, and the rest as they say is history.

So this is a quick pictorial summary of the timeline of thrombectomy that I just discussed, but to reiterate, very importantly, all of these were attempts at thrombectomy using technology that existed at the time that was not specifically created for or approved for thrombectomy. However, in tandem with that timeline there was considerable interest in actually creating devices that were made for thrombectomy, for large vessel occlusions, and that interest actually started back in the 1990s. So here is a picture that I got from this citation right here, for anybody who's interested in taking a deeper dive this is a really wonderful textbook that goes through the history of thrombectomy and where we are today. And I'm really going to spend the bulk of the time today talking about these first and second generation devices, the first generation device being the Merci device, second generation being the stent retrievers, because I think that's, frankly, what's most relevant to this audience today.

But a couple of points, one, although the Merci device, which I'll talk about in just a second here, although ultimately was not a success, I think it's important to note that the development of the device and the trialing of the device really paved the way for the continued evolution of the stent-triever, which is of course what we use in large part today. And this of course is generally speaking the story of how scientific developments happen in medicine, where you have things that are happening somewhat contemporaneously and then they come to this serendipitous head, and that's when the field takes a huge leap forward. And certainly acute stroke care has been no exception to that paradigm.

So before I get too far into what these different devices are, I did want to take a minute and just define the TICI score. Again, I'm sure this audience is very familiar with what it is, but just to say it out loud, TICI is an acronym, stands for thrombolysis in cerebral infarction. It is a corollary to the TIMI score, which we borrowed from our cardiology colleagues, which stands for thrombolysis in myocardial ischemia or infarction. So what is TICI? So essentially what it is, it's a radiographic score that assesses the patency of the target vessel that you just intervened on. And it goes anywhere from 0, which is complete occlusion, absolutely nothing making its way through, not a single red blood cell getting past it, all the way to TICI 3, which is complete normal reperfusion and normal patency of all the distal branches, and then there's everything in the middle from 1 to 2C. And it's important to establish that what is considered to be successful recanalization is a TICI 2B or higher, and this is actually how all the major trials also define successful revascularization. Just so that that's clear for everybody.

All right. So diving right in, the first generation device was the Merci device, and I'm sure many of you are familiar with or have at least heard of this device. Merci itself is an acronym, just like everything in medicine, mechanical embolus removal for cerebral ischemia, the device was actually conceived of in 1995 but it didn't actually become approved by the FDA for use until 2004. And at the time there was actually quite a bit of excitement about this device, mainly because it did not require the use of IA tPA or intra-arterial lytics in addition to it. And so people thought that maybe you have a device now that can achieve the same rates of recanalization without the same rates of symptomatic intracranial hemorrhage that we were seeing with IA tPA.

So what is it? Conceptually, it's actually quite simple. It is a Nitinol, Nitinol is just a metal alloy, it's a Nitinol corkscrew that is delivered on a micro wire and it comes through the sheath. The whole system is taken past the clot and then pulled back to engage the clot. The analogy that a lot of people will use is it's like a wine opener, it corks the clot and then the whole system comes out in bulk. Unfortunately, despite all that excitement, the Merci 1, which was the phase one study of the first generation of Merci devices, was not an overwhelming success. So less than 50% successful revascularization, again, by that we mean TICI 2B or higher, and up to a third actually did still have to receive intra-arterial tPA because of unsuccessful recanalization. And then most importantly, mortality approached almost 40% in these patients.

So why was this a... not a failure, but why was this not quite as successful as we wanted it to be? I actually personally have never used this device, but in speaking with other interventionalists who have, there's a number of different things people bring up. But I think that the thing that's cited the most often is that the device itself is a stiff, bulky construct, that can be a little challenging to navigate intracranially into very delicate vessels. And yet, despite that stiffness, the device, the actual corkscrew portion of it, the structural integrity falls apart after repeated use. So this is a good schematic of that, where you start with this really nice corkscrew shape which is designed to cork that clot and pull it out, and then after repeated uses it becomes just this Nitinol... almost like a spear. And you can imagine when you look at that that that's not going to be very effective for clot capture, it may actually cause clot fragmentation and distal embolization.

All right. So then we have the second generation of thrombectomy devices, which is now the new and improved stent retriever. No longer an off-label use of a device that was created for something else, but something that has now been modified and approved for use for large vessel occlusions. So what is the device? Well, fundamentally, it is a self expanding stent. And I'll show you a video in a second of what that means, and essentially it expands on its own, it doesn't require any additional balloon expansion. It's retrievable, which again is the reason why there was so much excitement behind the device. It comes on this wire that can take the device up, but more importantly can bring the device out of the body. It is also Nitinol based, that same metal alloy that the Merci device was made of, a lot of our devices are Nitinol based. And conceptually it's meant to engage the clot within the actual stent struts themselves.

And so here is the anatomy, if you will, of a stent retriever. What is demarcated as the usable length, that's really where the clot capture happens. There are some markers, Distally and Proximally, these are fluoroscopic markers that give us visual feedback that we have in fact deployed the stent in what we think is the right spot relative to where the clot is. Here is that all important pusher wire, again, allows you to take it out, but more importantly bring it back out of the body. And then it comes through this introducer sheath, right here. And this is just a schematic of what this looks like in the intracranial vasculature, again, you have a guide sheath, in this case they're employing proximal flow arrest, there's a balloon attached and inflated. Through that guide sheath is your delivery wire with your stent-triever engaged in clot, likely in the M1 segment. That's going to sit there for a couple of minutes and then the whole construct will come out.

Okay. This is a video of how the stent actually works in the body, this is borrowed from one of the educational websites that are out there. So just to orient everybody, this is the internal carotid artery coming up. This is the guide sheath that's positioned at the proximal ICA, and what you have going through the guide sheath is a micro wire. And that micro wire is actually going to make its way through the clot itself, the clot being let's say in the proximal M1, that micro wire is going to be positioned distal to the clot and that proximal M2 branch. And then over that micro wire is going to pass a microcatheter, and that microcatheter is also going to be, importantly, navigated past the clot. Once it gets to that point the micro wire comes out, and in its place we send up the stent retriever. The stent retriever goes all the way to the tip of that microcatheter, and then once it gets into position, the microcatheter is very gently pulled back, and as it's pulled back that stent flowers open.

And that's what we mean when we talk about a 'self expanding stent', it expands on its own as soon as that microcatheter is pulled back and it's deployed. And ideally it's deployed such that the clot that you're targeting is within that usable length of the stent that we had just previously described. Again, like I said, this will stay up anywhere from three to five minutes, depending on operator preference and frankly operator patience, and then eventually the whole system comes out.

So how did this device compare to our Merci device? Well, there were two randomized control studies that compared these two devices head to head, and they came out relatively contemporaneously with each other in 2012 in the

Lancet. There were two different stent-trievers that were trialed, one was the Trevo, one was the Solitaire. They're made by different device companies, there are some subtle differences in engineering and in terms of the device itself, but fundamentally both are stent retrievers. And so when they were compared to Merci, regardless of whether it was Trevo or Solitaire, the rates of successful recanalization, again TICI 2B or higher, were significantly higher with the stent-triever as compared with Merci. And the Modified Rankin score, the functional outcome at 90 days, which of course is really what we care most about, was also significantly higher with the stent-triever as compared to the Merci device. And so that really marked I think the final nail in the Merci coffin.

So that's a summary of some of the first and second generation devices that we have on the market, or at least the Merci that was on the market, the stent-trievers that are currently on the market. But there is still ongoing interest in device development and these are a schematic of some of the third generation devices that have since come out. And although robust data, the form of randomized control studies is still pending for some of these devices, I think it's pretty safe to say that in general we see that as our devices and as our technology gets better, our outcomes do get better. And I think this is a nice graph that, again, I pulled from the same textbook that I had mentioned earlier, and that shows this in real time.

So when you look back in 2005 with the Merci device and you compare that all the way to 2015 with the stent retrievers, and you look at rates of successful recanalization, you can see that the rates of TICI 2B, or 3 recanalization almost doubled really in a 10 year period, from sub 50% in '05 all the way to nearly 90% in 2015. And of course, this is not just solely because of the devices getting better, certainly I think we're getting much, much more sophisticated with our patient selection algorithms. And also, on the operator end, it's now become so widely done that there's much more operator comfort, much more operator skill, and so all of these things certainly factor into this very linear curve. But I do think that it proves the point that investment in ongoing development and evolution of these devices really does translate to better clinical outcomes.

All right. So in tandem with these devices that are being created to actually capture clot and bring it out of the brain, there's also interest in just simple aspiration or suction thrombectomy, which conceptually is very simple. So you have a guide catheter, again, positioned in the ICA. You have an aspiration or a reperfusion catheter that's navigated all the way to the proximal end of the clot, really to the proximal face of the clot. Once that catheter gets there the suction is turned on to negative suction, again left on for somewhere between three and five minutes and then the whole construct is removed, ideally with the clot captured and in place.

So the first set of aspiration catheters to actually be approved was the Penumbra system, and that was back in 2007. And the original data for primary aspiration thrombectomy recanalization rates were actually quite high, so they were showing successful recanalization rates approaching I think 80%, maybe even a little bit higher than 80%. Unfortunately, clinical outcome lagged a little bit behind, but that being said, the same narrative that we just talked about, as these suction catheters have improved over time, which they have, we've seen that translate to better and better clinical outcomes.

And this graph right here on the right side of the... chart, I'm sorry, on the right side of the screen, goes through all the different catheters that exist. And you can see there's multiple different catheters, different lengths, different size- [inaudible 00:28:49]... Different companies, different engineering. And to be honest, this is from 2019 so this is probably already outdated, I'm sure there's more catheters out there. But it just goes to show that we have so many different tools available in our arsenal for thrombectomy that helps us to get better and better outcomes over time.

So that is a story of how we got to where we are, and I'm going to spend the next few minutes discussing what the most commonly used current techniques are in terms of thrombectomy. And broadly speaking, again there's many, many different ways to do a thrombectomy, but broadly speaking there's two different types of strategies. There's either primary direct aspiration, or there is aspiration plus the use of a stent-triever, so I'll talk about each of these individually. So the primary aspiration or suction thrombectomy, the acronym ADAPT, I'm sure many of you have heard of that before, it stands for a direct aspiration first pass technique, and it was first reported in this paper published in AJNR, American Journal of Neuroradiology. And it's exactly this, what we just went through right here, where our catheter's taken up to the clot, placed on suction and then pulled out.

So I'm going to show you guys a video of what this looks like in a patient. Just to orient everybody, this is an AP view, so we're looking straight at the patient's head. This is the right orbit, this is the left orbit. The aspiration catheter is sitting right here, this is probably in the cavernous segment of the ICA, and going through it is a microcatheter micro wire system. And so I'll narrate as we play the video. So that micro wire microcatheter is going to go up. The MCA typically sits right around where the orbit is, so likely this is an M1 clot.

And that microsystem goes up first to serve as a scaffolding over which our aspiration catheter is going to go up. So once that gets up there this guy is going to try and make its way up into the M1. Sometimes you struggle a little bit because the distal ICA, especially near the terminus, can get a little tortuous, but we succeed. So here's that aspiration catheter now, likely engaged within the clot itself in the mid to distal M1. And once that aspiration catheter actually physically gets there, then the microcatheter system is going to be pulled out. And once that's out of the body, aspiration catheter gets placed onto section, left there for three to five minutes. And then the whole system comes back with the aspiration on and hopefully with clot captured within the catheter.

So that's ADAPT, and then the other strategy is a combination of stent plus aspiration. Some of you may have heard the phrase 'Solumbra', which used to be the term that we would use to describe stent plus aspiration, that came from a hybrid of the Solitaire stent retriever and the Penumbra aspiration catheter, that was like the celebrity mashup name that they came up with. Since then, of course, there's been more stents that have come out, there's certainly been more aspiration catheters that have come out. So it's a little bit antiquated, but the concept of using a stent plus aspiration is certainly still something that we definitely do a lot.

And again, conceptually, this is relatively straightforward. So you have a guide catheter positioned in the ICA, you have an aspiration or a reperfusion catheter that's navigated up near the base of the clot, and then a stent-triever is also deployed within the clot itself. And so this is a two tiered approach at trying to pull the clot out, the clot gets ideally captured within the stent-triever itself and then there's also negative suction being applied by your aspiration catheter. Again, three to five minutes being this magic time that we use, and then the whole system comes out in bulk, again, ideally with the clot captured in it.

So this is a quick video showing what that's going to look like. Again, just to orient everybody, this is an AP view, looking straight at the patient. Right orbit, left orbit. In this case here, the aspiration catheter has already made its way up, it's probably sitting at the ICA terminus, just based on where it looks on this unsubtracted view. And then through it, you could actually see if you follow this line, that there is a little dot right there at the tip. That is the microcatheter that's already been navigated up, and it's ready to go, ready for that Solitaire or whatever, stent-triever to go up. The patient in this video is going to move quite a bit so I'll try to narrate as I go. The actual unsheathing of the stent-triever and the pulling back of the stent-triever can be very stimulating, it can be quite painful for the patient. So often they'll little antsy on the table, so bear with me on this video.

But you can see here now, the stent-triever, it's making it's way up and it's going to get to that distal end of that microcatheter. And then as that microcatheter starts coming back, the stent-triever flares open, the patient obviously gets a little bit agitated. And then once the stent-triever is fully deployed you can see that aspiration catheter starts to be advanced even further distally. Again, you want to get that as close as possible to the clot itself to really improve your aspiration force on the clot. And then once it actually physically gets there it's going to sit there for a couple of minutes with the stent-triever capturing clot, and then the whole system will come back together out of the patients.

So, just to go back for a second, some people will often ask, "How do you decide between ADAPT versus this hybrid approach of stent plus aspiration?" There's been some retrospective studies that try to compare one versus the other, and I think the reality is that it comes down to the individual patient in front of you and the operator comfort. So if I have a patient with a proximal occlusion, let's say distal ICA, so ICA Terminus, or M1 segment of the MCA, and it's a relatively straightforward ICH navigate, I will often just defer to primary aspiration. Because then you don't have to mess around with a stent retriever, which just adds a little bit more time and complexity to the case.

However, sometimes the vessel is very, very tortuous and it's difficult to actually physically navigate that aspiration catheter up there, or it's too far distal and the aspiration catheter is just simply too large to be accommodated by a tiny little M2 branch of an MCA. And so in those cases some combination of aspiration plus stent, I think, can be very useful. So, I think the reality is both strategies can be employed, and I think it really comes down to patient anatomy, clot location and operator comfort and preference.

Okay, so that was mechanical thrombectomy. Again, just to go back to that first slide that I showed in the beginning, that was the overarching strategy of how we do thrombectomy. But there is also intra-arterial pharmacotherapy, again intra-arterial lysis, that has had a little bit of an undulating course in terms of popularity, so I want to present some of the information and the data for this as well. So first of all, what is IA? How is that delivered? So the concept again is not that complicated, a microcatheter is navigated usually as close as you could possibly get to the CLO itself and then tPA or lytic of choice is gently dripped into the vessel, and ideally the clot dissolves in that process. What are your drugs, what are the options that you have? There's a chart right here describing it which I won't read through, you guys can obviously read that. And most of them have been trialed in some form of an RCT for intra-arterial use.

And here on the left side of the screen is a chart going through some of what these randomized control trials have been, with various types of competitor arms, either IV tPA or placebo. I'm not going to get into the nitty gritty of these individual trials, because there's obviously quite a few and a lot of data right there, but I think there are some take home points that are relevant from this. So, one, in general intra-arterial lytics do have a higher rate of recanalization. However, this comes with a trade off of having a higher risk of symptomatic intracranial hemorrhage. And so it's certainly not something that most of us would reach for as our primary mechanism of thrombectomy, but there is an emerging interest in potentially considering it as a salvage therapy for particularly refractory clots that are a little bit distal, you can't access with a stent-triever.

So again, it depends on the operator, it depends on the clot, it depends on the patient, but there is potentially some use for IA lytics today. So, going back to the AHA Guidelines, this is the recommendation. It's a Class 2B recommendation that one can consider a salvage technical adjuncts, including for example intra-arterial lytics, to try and achieve a successful recanalization.

All right. So, all that said, I'm going to now just present a quick case, which I hope will synthesize at least some of these different concepts and then leave some time at the end. If anybody has questions, I'd be more than happy to answer. So this is actually a case that came from, I think, during my fellowship. Young woman, 48 year old woman, last known well at 11 o'clock in the morning and then five and a half hours later develops a pretty severe left MCA syndrome, right facial droop, right hemiplegia, left gaze deviation. Stroke scale is very high, it's a 26. Unfortunately not a candidate for IV tPA because she's outside of that four and a half hour window by the time she presents to our ER.

This is her non-con, I didn't really get into the ASPECTS score or how we define the ASPECTS score, but this is a good looking head CT. I don't even see any early evidence of infarct, certainly no hemorrhage. And then on CTA you can see that there is an occlusion in the left MCA, specifically that left mid M1 segment. Very quickly just to review the anatomy, and I apologize, anytime I put up a picture of the Circle of Willis I think there's always a collective groan from the audience, but I do think this is actually quite relevant and just to superimpose a picture onto the CTA to describe the anatomy here. So this is obviously our Circle of Willis. On the CTA this is our right MCA, this is our left MCA. Obviously in this patient there's a clot sitting in the left MCA. And then in the back of the brain you have your basilar artery with its PCAs coming off and the SCAs coming off. And then more anteriorly, you have your anterior cerebral arteries or your ACAS coming up and medial. That's it, no more Circle of Willis.

All right. So CT perfusion, this is her perfusion scan, again, I'm not really planning on getting too much into the details of perfusion imaging. Honestly, the imaging of acute stroke with the ASPECTS score, perfusion, et cetera, is a talk in and of itself that could be probably given over several hours. So I'm not going to quite get into the nitty gritty of it, but what do we see here? What am I looking at? So on this side of the screen, on the left side of the screen, is what would show up as dead infarcted core, and on the right side of the screen, what shows up is ischemic, salvageable, penumbra. And really what you want to see, as an interventionalist, is you want to see a patient with as little, ideally no core, as possible and as much penumbra as possible. Because what this tells me when I look at this is, whatever symptoms this patient is presenting with are attributable to ischemic, salvageable, and potentially reversible occlusion, that if I were to open that artery her symptoms might get better.

In terms of criteria for what we look at in terms of numbers, we look at both the mismatch volume and the mismatch ratio. Mismatch volume is the absolute difference between ischemic, penumbra and infarcted core, 84 is obviously a fairly large number. And then a ratio, we like to see I think anywhere from 1.5 or higher. Obviously this case is infinite because the denominator is zero, and I'm not going to get into any more math than that.

All right. So access, how do we actually do these procedures? In this particular case I elected it to go femoral, can you do radial thrombectomies? Yes, absolutely, 100% you can do radial thrombectomies. In fact, in certain circulations it's actually easier. So for example, if it's a posterior circulation stroke, and you have a right vertebral artery that you want to go through, a right radial access is actually a straight shot up, and so it's definitely... Definitely there is role for radial access in thrombectomy, even for carotids, et cetera. However, I think that at least for right now, certainly efficiency is key, time is key in these kinds of procedures, and the devices that we have are a little bit more tailored I think, in terms of efficiency, to come from the groin than from the wrist. But I do anticipate that that's going to change over time, as we switch to an increasingly radial first approach.

But anyway, in this particular case I chose to go femoral and I just wanted to very quickly go through what that vasculature looked like as well. So a schematic of the femoral anatomy, here's the femoral head, this is the right side, this is the femoral artery. So this is actually the external iliac, and as it crosses past the all important inguinal ligament it becomes the common femoral, and the common femoral then bifurcates into the superficial femoral and the deep femoral, and lying immediately medial to that is your femoral vein. What does this look like angiographically, so when we do a run? This is again the common femoral artery, this is actually our sheath or the sheath in this patient, this is not an artery this is just a foreign body that we put in. This is the common femoral, like I said, this is the SFA or the superficial, and the deep.

And then this vessel right here, the inferior epigastric artery, is actually one that is very, very relevant to us. And the reason for that is, the inguinal ligament is not something that you can see on angiography and so we need a surrogate for that, which actually turns out to be this vessel. It is very conveniently placed, where the inferior margin of the inferior epigastric, which is this little bump right here, correlates typically to where the inguinal ligament sits. So when I do a femoral run, I want to see my stick, I want to see my entry point come in below that inferior bump of the inferior epigastric. If it comes in at or above, that's when I would worry that if I don't get adequate hemostasis or adequate closure, this might be a patient who is vulnerable to a retroperitoneal bleed that is in a non-compressible site.

I always actually encourage trainees, providers, nursing, to get familiar with looking at the femoral anatomy, just because we take care of these patients in the ICU and the thrombectomies, or whatever endovascular cases we do, don't start and stop in the brain. And as everybody I think knows, there can be really serious complications that happen as a result of issues in the groin. So I always encourage people to look at these images and try to understand the anatomy, it helps you to better triage what's going on with the patient if there's an issue afterwards. All right, that's my soapbox, and I'll stop talking about that.

Okay. So in this particular patient, this is a left MCA, so we're going to go into the left carotid artery. Here is a view, it's a roadmap, that's literally what it sounds like. It's a map that allows us to then wire our devices up further into the head. So this is the common carotid artery on our AP view, again, looking straight at the patient, you can see the rib markings here that tell you you're looking straight ahead. This is the lateral view, this is where the shoulder would sit, you can see the back of the head, this is where the orbit and the jaw line coming down would sit. Common carotid artery comes up, bifurcates, internal carotid artery on the AP view typically starts lateral and then goes medial, here's the ECA or the external coming in, giving off its branches. And then on the lateral view you can see ICA coming up posteriorly and ECA coming up anteriorly, and they eventually swap as you go up further.

So we do the roadmap and then we put a wire all the way up into that internal carotid artery, and then our guide sheath, which I showed you guys earlier, that thing that sometimes comes with a balloon, that is then navigated either into the distal common carotid or into the proximal ICA. And I think in this particular case, I took it into the distal common.

Once that is navigated up into the ICA or into the common, we do a run. This is a common carotid injection that you see right here. I know it's a common carotid because I see branches of the external filling, in addition to the internal. Just to go through the anatomy here again, right orbit, this is where the left orbit would be sitting, top of the head. Here is the internal artery coming up, here's the cavernous segment that's going to make a turn at you, which is why it looks like that double density, Terminus, here is the anterior cerebral artery or the ACA A1 segment. This is where the anterior communicating would sit, and this is the ACA A2 segment. And then of course, here's the MCA with a clear cutoff that we saw on the CTA as well.

So, what was my strategy in this particular patient? I decided to end up doing a combination of stent-triever plus aspiration. And again, just to reiterate, this is what that looks like schematically, and this is- [inaudible 00:45:46]... looks like in the patient's head. So this is where the MCA sits, this is where that clot was sitting. You can see the stent-triever is open and deployed, those are the distal markers of the stent itself. And then here's the aspiration catheter that's been navigated up to the proximal end of that stent, sat there for a few minutes and then eventually came out. And fortunately for this patient, she had a really good clinical outcome and a really good radiographic outcome. You can see that all of these vessels are now open that clearly were not open before, I would consider this a TICI 3 recanalization, and she subsequently went on to do quite well.

So I'm going to stop there, that's really all I have. Thank you so much for your attention today, I hope this was helpful. I know that we spend a lot of time discussing the trials that go into why we do thrombectomy, but I think there's a lot to be said about the development of thrombectomy as a procedure in terms of the technical side of things, which of course I find really interesting and I hope this was something that was useful to you guys as well. So I'll stop right there and see if there's any questions.

Jeanie Luciano: Thank you so much, Preethi. That was wonderful, it was so comprehensive and you made even the anatomy so interesting for us. There's quite a few questions here, I'm going to combine the first two because I think they feed on one another. So when the catheters go through the clots, how do they not break them up and cause the clot to travel further downstream? And there's another question after that that says, what is the most difficult part of the clot retrieval that you encounter?

Preethi: Yeah, those are good questions. I'll start with the first part of that question, that's a great point and there is always a risk of clot fragmentation, in fact it certainly does happen. I think any one of us who do these procedures can tell you we've had cases where it starts off as an M1, you open the M1 and then you do the run and you see now there's clot sitting in the M2, and then you have to chase after that. So it's certainly a risk of these kinds of procedures. Unfortunately, there's no way to navigate our devices to the clot without actually crossing the clot, so it is a known potential complication. I'd like to say it doesn't happen that often, but I always say that it's a realistic possibility that we may have to fish out the clot from multiple vessels, depending on whether or not it embolizes.

As far as the hardest part, that's a good question. It probably depends on the patient, it depends on the anatomy. The steps of the procedure that I think you can get stuck on; the aortic arch actually sometimes can be very complicated in and of itself. There are many different... not many different, there's a few basic configurations of the arch which I didn't really get into that can make just navigation into the common carotid arteries very, very challenging, and often require a lot of different catheters and wires and exchanges, which can be complicated. Certainly there's been... I showed you guys that video of the aspiration catheter trying to make its way past that ICA terminus, and that can sometimes be very difficult to navigate. Sometimes if I can't get my aspiration catheter up, I'll take my stent-triever up, open the stent-triever and use it almost as an anchor to then guide my aspiration catheter up. And that's something that I think a lot of people do as well, but that can be tricky.

So it really depends on the case. And then sometimes you go in thinking this is going to be straightforward and one, I'm going to one pass and get out, and then seven passes later you're still staring at the clot. So, it just depends on the vessel.

Jeanie Luciano: Thank you. For sites that are sending you patients from an outside hospital, what can they do to help facilitate rapid treatment for you once they arrive at your facility?

Preethi: That's a good question. If they are going to come for thrombectomy specifically, things that can be very helpful. So often, not always, it's helpful to have an arterial line, if that can be placed. If you're just waiting for transport to come and you're just sitting around for that, it would be useful to put an a-line in. We try not to intubate our patients but sometimes you end up having to, depending on agitation issues. If you anticipate the patient is going to be very agitated or difficult to control, even if you don't want to intubate at your institution, I think doing things like a Foley can be useful. So I think those are the main things, sending off basic labs, those things really... I know they sound minor, but those are really valuable on our end when we receive the patients.

Jeanie Luciano: Thank you. You talked about TICI scores and patient outcomes, do you often see poor outcomes in patients who radiologically have a good TICI score or desired TICI score?

Preethi: Yeah, that's a good question. So the TICI score, it's just a radiographic score, all it tells you is my vessel is open or it's not open. But things that can still cause bad or poor patient outcomes despite that, obviously if they have a hemorrhage, just a reperfusion hemorrhage, that's just unfortunate, that can happen. Especially if they've had tPA on board, that is a known complication. Patients who come in who already have a decent amount of core, the CT perfusion that I showed you... I can try to go back to it. Here, there's no core here but sometimes we do take patients that come in with a decent sized core. And so even though you get a great radiographic outcome, you still have dead brain tissue that unfortunately you knew you were not going to reverse that with reopening the vessel. And so they may have the deficits that are there just because of that core, that have already been established. So I wouldn't say we don't see it, we certainly do see it, but I think in general, if you have good revascularization, the likelihood that they will do well is certainly higher.

Jeanie Luciano: Perfect. There's an anesthesia question, but I think you answered that in your previous question. What complications of endovascular therapy do you think are important to track and share with your team?

Preethi: Yeah. So the most common complication, the thing that I will always tell patients and families, is anytime we take catheters into the head there's always a chance of either worsening of the ischemic stroke that they already have and/or hemorrhage. And that hemorrhage could be subarachnoid hemorrhage, inadvertent wire perforations can certainly happen, especially in some of our more distal, smaller vasculature. There can be hemorrhage, just reperfusion hemorrhage that can happen, like I said, especially if they have tPA on board, or just reperfusion hemorrhage because they already have a large core, don't have a lot of collaterals. So I think those two things are important to document and to track.

I also think access site complications are really relevant. Again, I think we don't spend a lot of time talking about access and dealing with the things that can happen afterwards, but I think it's really important to be mindful of things that are happening, especially if it's femoral. The reason we're interested in radial is because there are generally speaking fewer life-threatening complications from radial, but femoral access, people can die with complications from the groin. And so I think tracking that is also really a useful metric when we do these types of procedures.

Jeanie Luciano: Perfect. There is a question here that goes into two lines. Okay. Can you go over the cutoff times for thrombectomy (I guess they're talking the 24 hour window), especially if being transferred from another hospital? Are there any scenarios where post 24 hour treatment would be appropriate?

Preethi: Yeah, I think we used to be, at least when I was in training and this was becoming... it was right at the surge of when all these papers were coming out. We were very strict with adhering to these time guidelines and time specifications. And obviously, we reviewed how in the AHA document it says you can go up to 16 hours, that's the Class 1 recommendation, up to 16 hours post last known well. Frankly, after six hours I think most people will get a CT perfusion, even if it's been 24 hours. And the CT perfusion, if it looks like this and the ASPECTS score is good in that I don't see a lot of stroke burden, I would still consider that patient for intervention. Especially because last known well is such a subjective measure, it's hard to sometimes gauge exactly what somebody's true last known well was. So for me, it's actually less relevant what the time is from last known well, and a little bit more relevant what the imaging shows, specifically with regard to the ASPECTS score and the perfusion scan. And if-

Jeanie Luciano: There's a question- Oh, go ahead. Sorry, go ahead.

Preethi: Sorry. No, I was going to say, if the time between let's say outside hospital to here, if that transfer... let's say they present at the outside hospital within four hours and by the time they make it to our institution it's... for whatever reason, there's transfer delays, and if they're outside that six hours, I will often repeat a CT CTP just to make sure we're not dealing with a completed infarct that's not going to benefit from thrombectomy.

Jeanie Luciano: There's two questions I'm going to roll into one since we're getting close to the end of the hour. These sound like certification questions. How do you handle two cases for endovascular therapy who present at the same time? And how long do you keep the post endovascular therapy patients in your ICU setting?

Preethi: Yeah, that's a good question. So how do we handle multiple strokes at the same time? That's a little bit institutional dependent, here we could in theory do two in tandem, if we needed to. We also have... at Main Line Health we have a partnership with Jefferson, and so if we truly did need to, if we had multiple cases at the same time, we could always have the option to transfer to our downtown Jefferson partners to take care of the thrombectomy. Again, whatever is going to be best for the patient, that's really what is factored into that decision.

As far as time in the ICU, so I always keep them till their 24 hour head CT is done, just to ensure that there's no hemorrhage, there's no delayed complication, after that I don't think you necessarily have to keep them in an ICU setting. Often these can be medically very sick patients, as we all know, stroke patients often have pretty significant cardiac disease and some other things, and they may have other systemic issues going on that may warrant critical care level of care. But from a pure thrombectomy standpoint, minimum 24 hours, and then from there depending on how they do they could potentially be bumped.

Jeanie Luciano: Perfect. There's a lot of kudos questions, not really comments, a lot of kudos to you for your presentation. One more question here, what is the role of MRI for thrombectomy candidates?

Preethi: Yeah, good question. I tend to not use MRI so much, I tend to use CT perfusion. I guess the one exception to that is posterior circulation, unfortunately the CT scans don't give us a really good look at the brainstem and the posterior fossa. So in those cases sometimes I will get an MRI brain, but I think for the most part CT perfusion is my go-to, in terms of making the thrombectomy decision.

Jeanie Luciano: Okay. That's all the time we have for questions. I want to personally thank you for the time and effort you put into this presentation, and your enthusiasm in doing so. And I'm going to hand you off to my colleague, Gino, to end out the webinar for us.

Preethi: Thank you, Judy.

Gino Mollica: Again, like Jeanie said and many others, thank you so much, Preethi, for your presentation today and willingness to give to the American Heart Association and everyone watching. We're going to be sending out a follow up email within 48 hours, and it will include a link to today's webinar. It's also going to have the certificate of attendance for anybody that might need it. If you're having issues opening that, go ahead and try it in Google Chrome, we found that to be the most successful, but you can always email me if you need anything else. We're also going to include in the chat a link to our American Stroke Month landing page. It has a link for all of our upcoming webinars, as well as some information on Nurses Week and Neuroscience Nurses Week, so we're going to make sure that gets added to the chat before the end of the presentation today. Preethi, thank you on behalf of the American Heart Association. Thank you everyone who was in attendance today, we hope everyone has a great rest of your day. We hope to see you online at our next webinar happening next week.

Preethi: Thank you so much.

Jeanie Luciano: Thank you again.