

**INNOVATIONS IN STROKE PREVENTION: AN UPDATE ON CAROTID STENTING
NEW YORK-PRESBYTERIAN HOSPITAL
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HERBERT PARDES, MD: I've always felt that the mission of helping somebody with health care when they're in trouble is as wonderful, as powerful, as important a mission as anything you could in life. And I think we're fortunate to have a great staff who feel the same way and carry it out every single day.

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HERBERT PARDES, MD: At the end of the day, we all can walk away and say, "This is our team, and it's a great team."

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JAMES F. MCKINSEY, MD: Good evening. Welcome to our webcast on innovations in stroke prevention: an update on carotid stenting. I'm Jim McKinsey. I'm the site chief of vascular surgery at Columbia University, a division of New York-Presbyterian Hospital System. To my right is Dr. Pierre Gobin, who is the director of Interventional Radiology here at Cornell. And to my far right is Dr. Bill Gray, who is the director of the Endovascular Therapy for Interventional Therapy at Columbia University. Tonight, Pierre, can you start us off and discuss some of the risks of -- for stroke?

00:02:02

Y. PIERRE GOBIN, MD: Good evening. Yes, if we could have the first slide. So stroke risks. A stroke is a major health problem in our country. 700,000 new strokes per year in the U.S., 80% of them being ischemic and 20% hemorrhagic. 160,000 deaths associated with stroke per year. Stroke is the third leading cause of death in the U.S.A., and the first cause of adult disability. Symptoms of stroke: the -- what is special about stroke symptoms is that they are sudden. They appear abruptly. They can last a few minutes to several hours. They can become permanent, of course, if it's not a TIA. There are several -- several types of symptoms. A typical one is

amaurosis fugax, and it can also be described as a transient monocular blindness. And it's a temporary -- sometimes can become permanent -- loss of vision in one eye. Then the other -- the other type of symptoms could be what are called transient ischemic attack, where the patient will have a sudden weakness or numbness in one side of his or her body. The face may become weak and someone looking at the patient will describe the face as twisted. Or finally, it could be a loss of speech or the ability to name objects, especially the -- in the left hemisphere in right-handed people. The definition of a stroke is a neurologic event lasting longer than 24 hours or resulting in permanent area of infarction on brain MR or CT. Now, what is the risk of stroke for carotid stenosis? It's variable according to if the stenosis is severe or just mild. In case of symptomatic severe stenosis, the risk of stroke is high and the risk of a recurrence, of the chance of subsequent stroke within the next year after the first event, is as high as 27%. If a stenosis is asymptomatic and severe, more than 60%, the risk of stroke over five years will be 11%. If it's a severe stenosis above 80%, then the risk of stroke over the next five years will be 15-20%.

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JAMES F. McKINSEY, MD: Some of the treatment options for carotid stenosis that can lead to stroke or to help prevent stroke is first medical therapy. Medical therapy was originally that of taking an aspirin a day, anti-platelet therapy, trying to prevent embolization. And that was some of the early work that was -- helped define the work when we compared carotid endarterectomy to maximum medical therapy with aspirin, hence the number of 27% that Dr. Gobin alluded to just a moment ago. We also now have added anti-- or cholesterol-lowering medications such as statins, which may further impact and act on the prevention of further propagation of carotid disease. Carotid endarterectomy was first described in about 1953 and is a way of surgically removing the plaque but does require a surgical incision in the neck and many times general anesthesia. Carotid stent angioplasty is the topic of tonight, and this is a minimally invasive approach in which we will access from the groin and treat the carotid artery remotely. Carotid endarterectomy as shown here is a surgical exposure of the carotid artery in which an incision is made after clamping the artery above and below the area of stenosis, opening the artery up, and as shown here, completely removing the plaque from the carotid bifurcation where the majority of the disease occurs. We will use special magnifying glasses to feather out the plaque and assure there's a very good endpoint both at the end of the plaque and at the beginning. Once we've completed the removal of the plaque, we will then put a patch or primarily close the artery, thereby reallowing restoration of flow to the brain. Many times during these procedures, there may be signs of low blood flow, at which a shunt would be placed to maintain cerebral perfusion of blood flow to the brain. At New York-Presbyterian Hospital Systems, we looked at the results of our carotid endarterectomies, and over a five-year period studied over 500 carotid endarterectomies. In that, we looked at both high- and low-risk patients based on their anatomy as well as their medical comorbidities, including coronary artery disease, pulmonary dysfunction, and renal dysfunction. We looked at 38 outcomes as endpoint for both stroke as well as other morbidities. And what we found is that we had a very low rate of stroke. No strokes occurred in the low-risk patient and only 0.9% risk of stroke in the high-risk patient population. The most common complication was a neck hematoma in 2.5% of the cases. So how do we assess those people that are high-risk for carotid stenting? And there's certainly a difference between carotid endarterectomy high-risk patients and those at risk for carotid stenting. Carotid endarterectomy high-risk are those patients with significant coronary artery disease. Again, many times general anesthesia is required, though we can do it under local anesthesia. Severe lung dysfunction, so patients can't lay flat on an operating room table, and prior surgery in the neck, such as for cancer

or previous carotid surgery. And finally, neck irradiation. All these factors make patients higher risk for carotid endarterectomy and certainly patients we would consider doing carotid stent angioplasty upon. The technique for carotid stent angioplasty is multifactorial. First is the access is generally done, performed, from a groin access, so a small puncture in the groin with a catheter a little bit larger than a piece of spaghetti. The catheters are then introduced into the main blood vessel and up to the chest and allow for imaging of the carotid arteries, where we can then intervene. Once we have imaging of the carotid artery and access with the special catheter called a sheath, we can then place a filter, or cerebral protection device, to prevent any small fragments of debris from the carotid artery to embolize the brain and potentially cause a stroke. There are several ways that we can do cerebral protection, and we'll discuss that in just a moment. The catheters are multiple shapes, depending on the anatomy of the aortic arch in the carotid, and they vary from a very slight angle, as you can see at the top of the slide, to a very acute angle or even a double-curve type of catheter, as you see here for more complicated anatomy. All these catheters will allow us to access the vessels and then place a sheath, which is a larger catheter, which will allow us to work from that and keep a very stable environment to pass balloon stents and filters during the carotid stent angioplasty. The cerebral protection can come in several different forms. There are commercially available devices that have filters that can allow us to capture the debris beyond the area of the carotid plaque during the time of the carotid stent angioplasty. In special cases, we may actually use a distal occluding balloon as seen in the bottom of the field, and there's currently work being performed on actually systems that will reverse flow to protect the brain during the time of carotid stent angioplasty. Why is that important? Well, here is an example of a carotid stent that was performed and then the distal atheroma that was collected from that carotid stent angioplasty. So certainly the need to have a distal protection during the time of the manipulation is important to help prevent embolus from going to the brain. Now, certainly once the stent's in place, the atheroma is trapped behind the stent and is much less likely to embolize. Once we have the cerebral protective device in position, we will then dilate the artery to allow passage of a stent, place the stent, and then come back and further dilate that to maximally open the artery to allow flow to the brain. This is an example of the different types of stents we can use. Some have closed cell, as seen on the top, of a stainless steel variety, and then others have an open cell, meaning there's breaks between the connections of the stent to allow a little greater flexibility, and then finally the closed-cell design, which helps trap and prevent further embolization after the time the stent's been implanted. Bill, perhaps you can describe the angiographic procedure in more detail for us.

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WILLIAM A. GRAY, MD: Thanks, Jim. The -- the next -- the steps in the diagnostic workup of the patient and on catheterization table include an angiogram. I believe we're in relative agreement here at the two institutions that both a carotid angiogram bilaterally as well as intracranial angiography is appropriate for most of the patients undergoing carotid stenting. Exceptions to that will typically involve patients who have poor renal function and in whom pre-procedural imaging might have already given us the answers that those studies might give us. Bilateral angiography is performed with the catheters that Jim mentioned previously, and they are selected depending on the patient's anatomy. Intracranial imaging is performed not only to get a pre-procedural picture of what's going on, really understand what vessels are present, be able to compare them to the post-procedural results, but also to understand any incident intracranial pathology that might have bearing on whether or not the procedure should be done, whether the patient's symptomatic from that pathology and so on, and what the collateralization

patterns are. There are different ways of collateralizing the carotid circuit, both extracranial -- that is, from the external carotid artery -- to the intracranial circuit, or intracranial to intracranial, which our next slide shows us the majority of which. The intracranial collaterals are largely distributed by the circle of Willis. The circle of Willis is the reason that patients who have tight carotid blockages can go for many years and even become occluded without any symptoms, because flow is distributed in the circle of Willis from the other various contributors, that is, the other vertebral arteries and the carotid artery. The circle is constructed of both the anterior and middle cerebral artery portions as well as the anterior communicating artery and the posterior communicating artery, as well as vertebral circulation. The circle of Willis, unfortunately, is only present in about 50% of the patients, so it's not always a reliable circuit, but it is there for the most part to protect us from stroke in patients with severe stenosis. It turns out that only about 5% or maybe 10% of patients who have a blockage get symptoms because the blockage is restricting blood flow. Most symptoms of TIA and stroke that Pierre mentioned previously are related to embolism from a plaque that ruptures. We have a case to present today, and we're going to base our commentary and discussion around the case primarily, and then we'll have some data sets afterwards to talk about. The patient was a 71-year-old gentleman who was asymptomatic. At the time of a typical physical examination at his primary physician's office, he was auscultated to have a bruit, and a follow-up duplex of high quality at a certified lab demonstrated Doppler velocity was greater than 80% in severity on the one side, the other side not being significantly stenosed. Because the Doppler was of good quality, we did not engage any other imaging, such as an MRA or CTA, but I wonder if Pierre and Jim might want to comment on whether they routinely get MRAs and CTAs or whether that's something that they're comfortable minimizing in an asymptomatic patient. In a symptomatic patient, I think it's less of a question. We need to get that cross-sectional imaging.

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JAMES F. McKINSEY, MD: Well, certainly we use the duplex very liberally because I think it's a non-invasive way, without a contrast load, low cost, that lets us see very well the carotid itself. There's limitations certainly -- I can't see into the arch and I can't see into cranial views -- but to say is there a significant stenosis, especially in the asymptomatic, it's my procedure of choice. And most of the time, I will not go on and do an MRA or a CTA or a diagnostic angio based on a good-quality duplex; I'll go straight, if I feel it's appropriate, to doing the intervention with carotid stent angioplasty or endarterectomy. Pierre, what do you do?

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Y. PIERRE GOBIN, MD: Well, I'm a neuroradiologist, so I will do an MRI. I will do a brain MRI and a brain MRA. The MRI will tell me if there is already -- if a patient had a stroke and is asymptomatic infarct into this territory, because this may change my indication and make me treat more liberally even if a stenosis is, say, only 65, 70%, where I would not treat an asymptomatic patient. But I would treat a patient that is MR -- which MR is symptomatic. Then I will do a brain MRA also because I like to see the intracranial circulation before I start a case. It's an information that we could get from the angiogram also, but I like to have it before starting the case.

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JAMES F. McKINSEY, MD: Yeah, I think that's an important thing also is that with the current role of using carotid stent angioplasty, we can get a lot of that additional information that we never got with carotid endarterectomy. We never -- if we just did it based on a duplex, I never knew what was going on in the chest, I never knew what was going on in the brain. So I think,

you know, by the combination of duplex and then going to carotid stent angioplasty, you can get all the information.

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WILLIAM A. GRAY, MD: There have been studies that showed with the duplex alone operating, even if there was intracranial disease, turned out that they didn't have a clinical consequence, so that the knowledge of intracranial pathology didn't really help decide much. You know, the other thing that's important, I think, as we get new technologies having to do with flow reversal or flow occlusion, that the collateral circuit may be important for procedural planning purposes. We may choose a filter in one case or a flow reversal in another, depending on what the anatomy looks like both tortuosity as well as collateral contribution, so I think more and more we'll probably be doing -- as those choices become available to us, more cross-section imaging. Next, you know, we're going to start looking at the video. The first video frame, we'll be looking at the arch anatomy. The types of arch we'll talk about here. Pierre will outline that for -- Jim actually will outline that for us. And the various access techniques. The current access techniques are, as Jim mentioned, usually from the femoral artery. That's because most of the catheterizations were performed there. In cases where femoral artery access isn't available for obstructive or other disease, radial artery or brachial artery access is available and is typically done with either guiding-type catheters or sheaths, which are placed through support of wires. Interestingly, in Europe now, there are some direct carotid access programs going on: small incisions being made in the neck and catheter delivered stent with embolic protection. So I think we're going to see a Back to the Future kind of evolution of access for cryostenting which will include not only the transcatheter brachial and femoral but also potentially direct access to the carotid, and that's still to be vetted, but we'll see how that plays out. So if we can go show the first video loop, we can walk through the first procedure. So this is the arch angiogram of this particular patient. You can see he's had prior bypass surgery and he has a reasonably favorable arch. Pierre, do you want to comment on his arch, his arch anatomy, and as we talk about that a little bit, maybe some of the specific features of arch angiography that is not only what type of arch the patient has but the concomitant angiography pathology of disease and so on and whether there's other information on the angiogram save for the arch that's important to you.

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Y. PIERRE GOBIN, MD: Yes, so the arch that we saw, it's what we call this easy arch, where the vessels are not too tortuous. The supraaortic vessels are coming off the top of the arch, so we know that catheterization is not going to be too difficult in that case. I like also to see if there are some calcifications, and with calcification you can see it actually better on a CT than on an angiogram. If there are some arch calcifications -- if those calcifications are severe, actually, you may reconsider an indication of carotid stenting and the surgery could be much safer than going through a very calcified and tortuous arch. Jim, do you want to commence on the following?

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JAMES F. McKINSEY, MD: Thank you, Pierre. Yeah, I agree. I think that, again, is some of the expertise that you have to have as you're doing these procedures is you have to be able to look at it and say this is a safe arch to do a carotid stent angioplasty and this one may not. And I think if you try and push an unfavorable position, especially if you're inexperienced, that could lead to devastating results. As you start looking at the arch, the other thing you have to keep in mind is it's not just a straight tube, it actually can have a significant counterclockwise rotation as you come in. And as you start using your catheters, you have to count on that as you start positioning them. Here is a more complicated arch that certainly can be performed but does require a little

additional expertise in doing the procedure. But you have to be able to come in and know that counterclockwise rotation as you place your catheter in sheaths. As we try and describe the different types of arches, this is what we look at. We look at the dome of the arch, as Pierre alluded to, but the great vessels, meaning the ones coming to the carotid arteries as well as the arm, if they come off the very top of the dome, that's very favorable to address our catheters with low probability of causing any injury to the arch as they come through or release of thrombus or calcification. Once you have it going below that level at the dome of the arch, it becomes more complicated. And as it goes down, as you see in this example, below the lesser curve of the arch, this is what we call a Type 3 arch, and that's probably the more complicated arch anatomy, and one that you should have significant experience before you tackle doing a carotid stent angioplasty. Bill, could you perhaps go to the next video?

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WILLIAM A. GRAY, MD: Yeah, let's roll the next video. We have the beginning of a selective angiogram. So now we've taken a catheter and we'll put it in the right common carotid artery. If that video can come up -- there we go. And what you see here is this is the unaffected side, and we take pictures here to confirm our duplex analysis both of this side as well as the other side. And so we want to understand -- make sure we're not getting sidetracked with wrong information. Here's an intracranial look, and you can see to the left of the screen a middle cerebral artery with its appropriate branches, the bifurcation of the internal carotid there, and then the -- moving rightward on the screen, the anterior cerebral artery on the right and the anterior cerebral artery on the left. Here you can see both anterior cerebral arteries and the pericallosal vessels, and we understand then that there is crossover through the anterior communicating artery from this unaffected side to the affected side, and I think, you know, this may be a good time to ask Pierre what he thinks about the value of contralateral or even intracranial angiography as much as that it does require another intubation, a little more contrast. Although there's modest risk, I think it's worth commenting on the value.

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Y. PIERRE GOBIN, MD: The risk is minimal except if you want to reduce the contrast load, if your patient is in renal insufficiency. I always image the contralateral side. It will, as you say, confirm that this contralateral side is healthy or that the stenosis is only mild. And it will also tell us about the collaterals. And the collaterals are important because here in your case, we see that the left anterior cerebral artery is fed by the right side, so is it hemodynamic or is it anatomic? And if it is hemodynamic, it's important, because it means that there is a hemodynamic compromise on the left side, so it means that if this patient has a severe -- has a severe stenosis with collaterals coming from the contralateral anterior carotid artery or from the posterior cerebral arteries, this is a patient that could be subject to reperfusion hemorrhage and it's a patient in which blood pressure should be very tightly controlled after the case. On the other hand, if there is no need for -- for -- for peel or for collateral through the circle of Willis, then you know that there is no hemodynamic compromise, so that patient does not have this risk of reperfusion hemorrhage.

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WILLIAM A. GRAY, MD: Do you -- you mentioned an anatomic reason to have the crossover to the anterior cerebral artery. Maybe you can comment on that and its relationships to isolated territories and what that might mean to the patient and the procedure.

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Y. PIERRE GOBIN, MD: Yeah. This is what you described at the beginning when you described the circle of Willis for when you're -- how those -- there a lot of anatomic variations, and some segments could be hypoplastic. One very frequent variation is when one A1 segment -- first segment of the anterior cerebral artery -- is hypoplastic, so then the trilateral carotid artery will give both anterior cerebral arteries.

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WILLIAM A. GRAY, MD: Let's move to the next video segment. This next catheterization is going to show us the index lesion. It's going to be an intubation of the left carotid artery, and you can see that here. Just describing this, you can see a lesion past the bifurcation and in the area of the proximal portion of the left internal carotid artery. The distal vessel is straight and favorable for a filter device. Jim, you know, I want you to comment on the measurement here, and this is obviously a tight lesion, but the bigger issue is what's the appropriate measuring standard and how easily can we be confused by that. And then lastly, maybe you want to comment: you know, this lesion looks like it's mostly in the internal carotid artery, but I know as a surgeon you know that that's not the only place this lesion is. It originates in other places and we need to consider that as we do a stenting procedure.

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Y. PIERRE GOBIN, MD: Can we run the video again?

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WILLIAM A. GRAY, MD: One more time.

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JAMES F. MCKINSEY, MD: Well, while they're getting the video -- while we're -- let me take your question there, Bill. I think the issue really is how we measure the degree of stenosis, because so much of our data is based on calculation of the degree of stenosis. So the tighter the lesion, the more likely it is to have a potential embolization and a stroke from it. So we need some form of standardizing the way we actually measure the degree of carotid stenosis. The NASCET group actually proposed a very simple and straightforward way of measuring degree of stenosis that's uniform. So what you actually look at is not the -- it's not the matter of looking just at the stenosis and saying, "Oh, it looks about 80%." What you do is you measure the degree of stenosis and then you measure where the artery becomes more normal, where the walls become parallel distal to or beyond that area of stenosis. And then you calculate that by simply dividing the degree of stenosis by the more normal distal artery. So if you run that video again, we can see that she -- this patient has a very critical stenosis just beyond the division of the carotid artery, and then when you come back normal, it would certainly would be in the 80-90% range with that tight stenosis. Now, I think the other question that you had, Bill, is really how far does the plaque go. And what we've seen surgically, and certainly from the majority of the plaque that we see is that that plaque starts at the flow divider. So where the carotid actually splits to go to the brain or go to the face, that's where the plaque starts actually depositing. And it deposits in more or less a spiral way, so it starts from the common carotid artery and then goes up into the internal carotid artery preferentially, mainly starting at the wall opposite the flow divider. And so it's important when you're treating these lesions that you actually treat not only the internal carotid artery but you extend down into the common carotid artery, because that area will also eventually develop atherosclerotic disease and potentially cause a failure of your carotid stent if you haven't treated it appropriately. And if you talk about how we actually look at this, here's a study that actually looks at when people go in just eyeball the degree of stenosis and then actually put calipers to it, and what we've found in all these cases is that when you look at the degree of stenosis and just

estimate, you tend to overcall the degree of stenosis when you actually compare it to the precise measurement. So I think it's important that when we're looking at these carotids that we actually take the time to measure it so we have a standardized way of comparing it to the trials that are now ongoing so we know exactly how to risk-stratify our patients.

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WILLIAM A. GRAY, MD: You know, and as we talk about the trials in the near-term future in this discussion point, you're going to know -- you need to know that all the trials that have ever been done in the ones we're going to talk about have all had a core angiographic laboratory which has defined the stenosis by calipers, by a quantitative angiogram so that the patients who are treated, we understand better really who those patients were, not just eyeballed. Let's go to the next video and we'll talk a little bit about the left intracranial circulation. We would expect, Pierre, to see something here which is missing the anterior cerebral artery. And in fact, we are missing anterior cerebral artery. On the right side of the screen, you see the middle cerebral artery filling normal, maybe a little delayed in flow because of the tightness of the lesion, but the anterior cerebral artery doesn't fill at all. And what was not done during this procedure, and maybe you want to comment on a little bit, is an analysis of the posterior circulation intracranially. We did get a look at it in the arch angiogram because of the origin of vertebrals in that picture, but given that we might have an isolated territory or may be contributing from the vertebral arteries, do you think that's important in a case where we've selected a filter as our primary mode of embolic protection, and what do you ordinarily do in these cases?

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Y. PIERRE GOBIN, MD: Looking at the posterior circulation?

WILLIAM A. GRAY, MD: Right.

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Y. PIERRE GOBIN, MD: Yeah, it's an interesting question. Certainly a risk that you take in placing the catheter into the subclavian artery, just doing an x-ray, visualizing the one vertebral artery, the left one, it's easier to see another posterior circulation. The risk that you take is so low that I think it's an information worth to get, so when I don't have a very good view of the posterior circulation from my pre-procedure MRA or CTA, then I like to take a look at the posterior circulation and do a vertebral artery or a subclavian injection.

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WILLIAM A. GRAY, MD: Jim, how do you position yourself in terms of vertebral artery injections in this case in particular but in general? How often do you routinely select or subselect?

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JAMES F. McKINSEY, MD: Yeah, I think to subselect the vertebral artery I will rarely do unless I really feel like they have vertebral basilar symptoms. I will do an arch angiogram and then look at the subclavian artery and the vertebral artery from there, and if necessary, I'll selectively catheterize the subclavian artery and do the angiogram. To instrument the vertebral, I think you're putting the patient in slightly increased risk of an embolus in the posterior stroke, and unless there's a good indication for doing it, I generally don't do it and I do it more from the subclavian.

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WILLIAM A. GRAY, MD: Yeah, I have to admit that I don't routinely do a vertebral angiography either in the subclavian or otherwise. In this case where there might be a posterior contribution or knowing whether there's a posterior contribution, it would be interesting. I'm not

sure it would change too much in a filter case the choice or selection of equipment. Balloon angioplasty is going to be up and down in a few ten seconds, the patient may have loss of consciousness or seizure related to that, but I'm not sure we'd do differently, or maybe you -- maybe I should ask the question, would you do differently? Would there be some reason to potentially put the patient into an endarterectomy? Would you do that if you found that there wasn't an adequate circulatory collateral to that segment, if it was isolated?

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Y. PIERRE GOBIN, MD: No, I would not change what I would do during the procedure. I would place a filter and do the balloon inflation and do as fast as possible anyway. But it may change my post-procedure management under -- if there are PO collaterals from posterior circulation to the MCA or from the anterior circulation to the middle cerebral artery, then it's a sign of a hemodynamic compromise and then I will control the blood pressure of the patient more tightly after the procedure, make sure that the patient is not hypertensive after the procedure, at least for the next 24 hours.

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JAMES F. McKINSEY, MD: I think the only other concern I would have is if I was using either a balloon occlusion type of embolic protection device for those very tortuous hard-to-cross lesions or a flow reversal. If I felt I had some concern about the degree of collateralization from the contralateral carotid and I didn't have good vertebral visualization, I would probably go more toward a filter device than a flow reversal or a balloon occlusion.

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WILLIAM A. GRAY, MD: Or you'd know for sure what the collateral was.

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JAMES F. McKINSEY, MD: Right.

WILLIAM A. GRAY, MD: Okay, let's go to the next video. The next video is going to be angiographic description, really, of the sheath access into the carotid artery. And what you can see here is we have a TAD wire, which is an .03018 distal tip wire which transitions into an .035 wire. And that's been placed through the diagnostic catheter into the external carotid artery. This can be done either on a road map or with a still-frame picture. We usually put the patient -- the II in the most appropriate place to divide the vessels or show the bifurcation. And then we back out the diagnostic catheter and the short sheath and we put in a long 6-French sheath, which you can see being transitive here into the common carotid artery. What you'll see next is both the sheath dilator as well as the wire being removed right there, and the sheath is then put probably about four centimeters or so below the bifurcation to provide adequate access. One of the downsides of doing difficult access with these smaller caliber sheaths is that it's easy to lose that sheath if it's not up high enough. Pierre, you know, maybe you want to comment on the different modes of sheath access, and, Jim, the same way, sheath versus guide, French size, access -- alternative access from femoral arteries, radial arteries, and so on.

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Y. PIERRE GOBIN, MD: All right, so a wide question. Well, a 6-French sheath, which corresponds to an 8-French guide catheter, are all what are necessary now using modern stent, more modern devices, so it's really small. I like to do -- like everyone, from the groin preferentially. I would be very careful if the iliac arteries are very tortuous not to use a sheath that is too stiff there, because you can have some complication at the iliac -- iliac arteries. So I would prefer to use a shuttle-type catheter rather than the regular 6-French sheath if those arteries are very tortuous. Then another big question that we could discuss now or later is when

should we chose -- another problem, the femoral approach? When should we use a radial approach or even I think over the last five years I've done one carotid approach. It's a completely exceptional case, but certainly we shouldn't recommend for general practice. But choosing a radial approach, I will say about close to 10% of cases I chose a radial approach, and especially in Type 3 arch or when there are some arch calcifications.

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JAMES F. McKINSEY, MD: I think certainly that's a good use for the radial approach and you're very facile at doing it. Carotid approach, I think we've all had a significant concern about, and some of the earlier studies were actually done with a carotid access and were found to have a significant result in complications, so except for very, very exceptional issues, I'm not inclined to do that. I think for the common carotid artery, you know, there is also another complication that can occur with that or a compounding variable is if the external carotid artery is occluded. If that's occluded, then you're going to have difficulty, because normally what we do, as Bill showed in the last video, we actually access into the external carotid artery with our wire and then pass our catheter and sheath up into the common carotid arteries using the external carotid to help stabilize our wire and our catheter. When that's not available, that becomes more of an issue. So if we talk about the common carotid access, I think generally I use a less curved catheter that allows easy access into the common carotid artery itself. Once the catheter's engaged, an .035 angled wire I'll place into the common carotid, and I personally use more of the floppy wire while I'm accessing until I've got good position. And then the catheter is advanced over the glide wire into the common carotid artery. From there, the wire is advanced under road map into the external when it's available. And then the common carotid artery lesions, if it goes straight into the internal carotid or if the carotid stenosis actually is of the common, I'm hesitant to try to pass a wire through that stenosis for the risk of embolization and potential stroke while I'm trying to access with the sheath. So what we will do is -- and here's a case of a sever calcific lesion, one that would certainly be a concern for possible embolization -- that the external carotid artery's already occluded. So you have a very focal lesion but no real place to pass the catheter beyond that stenosis without risk of embolization. So what we'll do is we'll come in, we'll put a sheath into the aortic arch, and then pass a catheter -- a Brady catheter -- into the common carotid artery and then use a stiff wire such as an Amplatz with a very short floppy tip that'll allow me to get a reasonable seat within the common carotid artery. Now, care has to be taken when you use these very stiff wires for risk of dissection, but many times this is the only way we're actually able to access that vessel. Once we do that, then you can pass your filter with a sheath in the common carotid artery, do your carotid stent angioplasty with filter protection, and as you saw here, we were able to get a very good result. So the absence of an external carotid artery does not negate your ability to do carotid stent angioplasty.

00:37:59

WILLIAM A. GRAY, MD: Great. So we're going to move to the next set of videos here. The next one we're going to see is the filter being placed. In this particular case, you might wonder if filter placement would be easy, hard, or somewhat encumbered because of the lesion severity. The tortuosity isn't particularly difficult, but the lesion is quite tight. So if we can run the next video segment. So here's the filter. The filter is constructed with an .014 wire at the distal tip. It's relatively floppy. And in this case, in this particular case, the filter flew right through without any real difficulty. I think the key there is keeping the tip free and clear of the lesion. This one has a peel-away type of cover that allows the filter to then pop open once the cover is pulled back. You can see the cover being taken out of the screen there. And as it peels away, it's taken

out of the body and the only thing that remains behind is the .014 wire, the filter basket at the top, and the tip of the platinum. Where we typically will put that in the petrous portion of the carotid artery largely because we want to make sure that placement allows us to have a bumper, if you will, so that the filter won't go too far distally and the only thing our assistants and ourselves have to worry about is pulling the filter back too far. Pierre and Jim, you know, I think that it's worth commenting on, A, in this case we had no trouble getting access into that lesion with the filter intradistal internal carotid, but suppose you did, what are your methods for getting through that? And I'll now pose a couple of different questions. One is angulation. Sometimes the carotid comes off almost at a 90-degree angle from the common and the internal transit into the lesion makes it difficult. And so angulation becomes problematic, so there may be some filter tricks or different types of filters you like to use. And then secondly, if you do have trouble even getting into the lesion because the lesion's either too tight and/or too calcified to pass a filter without obstruction, you know, what do you do there, what are your methods? And then lastly, we should talk about, and we can come back to this at the end, the development, the evolution of flow reversal, which is now in study in this country. We're doing a trial at this institution on flow reversal, and we -- I think it's probably worth talking about that as well. But let's talk about the filter issues first. Angulation and lesion severity first. Jim?

00:40:15

JAMES F. McKINSEY, MD: Well, I think certainly we will look at the area of angulation. And you have to be looking at it after you've got your sheath in place. Because certainly that can change the anatomy just by simply by placing the sheath into the common carotid artery. And also should be pointed out that before I ever engage any catheter into the carotid, we anti-coagulate the patient, generally with heparin, but certainly there are many agents that can be used. Once we're there and we see that there's a tight angulation, most of the filtering devices have a malleable tip on them, so I will then mold the tip such that it will look like it will take that turn into the area of angulation. We can do that and many times that will allow the filtering device to pass. Each filtering device has its own characteristics. One size does not fit all, and so it's important for the interventionalists to know what each filter can and can't do. If after trying the right filter and the angle's just too acute, you can do something called a buddy wire, where you actually pass a second wire through the area of stenosis using an angled catheter. We showed earlier some of the many different catheters that are available, and with that angled catheter, we're able to direct the wire into the internal carotid artery. That will help straighten and give a path to pass the filter device through, and there actually is a filter device that will cross over the existing wire to allow you to implant the filter beyond once you remove your starting wire. I think that's of significant help using the right-angle catheter to help get into position, the buddy wire and then the right filtering device. Pierre, what do you...

00:41:52

Y. PIERRE GOBIN, MD: Well, first I would just reconsider the entire procedure. If it to me looks too difficult a lesion, too calcified, too tight, let's say can this patient be treated with surgery? So then if I decide to proceed with the carotid stenting, there is something that I like to do in difficult cases, is to catheterize the stenosis with a regular micro wire and a regular micro catheter. The micro catheter has to accept the filter wire of the EmboSh-- I will use the EmboShield. Sorry, I'm giving a commercial name here. And then when I have the wi-- so I will pass the stenosis through a -- with a micro catheter and a micro wire; almost no stenosis would resist to this. I will be always able to pass a micro catheter through there. Then I would advance the wire, the stop wire of the EmboShield and then perform the procedure with this wire.

00:43:01

WILLIAM A. GRAY, MD: Go ahead.

00:43:02

JAMES F. McKINSEY, MD: I think certainly there's been times where even .014 wire I found to be occlusive, so sometimes you do have to do a pre-dilatation. And that's where you put a very low profile balloon, .014, go up there and just very gently dilate just to let your filtering device cross through. And I think you do bring up a very good point is what makes high risk for carotid surgery does not necessarily make high risk for carotid stenting and vice-versa. Carotid stenting contraindications may not negate carotid endarterectomy. So you have to keep both in mind.

00:43:33

Y. PIERRE GOBIN, MD: This is absolutely essential. That's why you need to be able to do both or work in a team where you always know what your colleague can do and be always able to offer the best choice for the patient. If at the last moment you are doing an angiogram and you don't like what you are seeing, there is absolutely no shame in going back, stopping the procedure and refer the patient to your colleague vascular surgeon.

00:43:59

JAMES F. McKINSEY, MD: Sometimes I feel like I'm schizophrenic: I'm talking to myself on which way is the best way to go.

00:44:04

WILLIAM A. GRAY, MD: You know, it's worth just you commenting, Pierre, because it really tends to occur within the neuro intervention neurosurgical circles, and I'm not going to put you on the spot here, but there are some people who don't believe that embolic protection is necessary. And to be fair, we don't have randomized trials that says that embolic protection is appropriate or necessary, and yet today the government only sponsors those types of procedures that are covered with embolic protection, so maybe the comfort levels with neuro intervention is primarily because they know what to do if there's a rescue situation, but maybe you want to comment that there's another reason or maybe you support that, or otherwise. I'm putting you on the spot, so...

00:44:43

Y. PIERRE GOBIN, MD: No, it's fine. This is fine. It's a very good question. I'm actually surprised when some of my colleagues argue that embolic protection is not necessary. There are, I mean, very respectable people that I respect but I just strongly disagree with them. And I must say that I would not perform a carotid stenting if I cannot have a form of embolic protection, be it distal or proximal. We have many choices now. As you say, we are in the -- are more is the idea of proximal protection, so we can offer to all patients all the choices of embolic protection, and I would not do a carotid stenting if I cannot offer one kind of protection.

00:45:25

WILLIAM A. GRAY, MD: Do you feel the same way, Jim?

00:45:27

JAMES F. McKINSEY, MD: The -- yes. 99% of the time, I agree. If I've got a very tight fibrotic re-stenosis, I would consider doing -- and I actually had this case where I had to do a dilatation just enough to get flow so they could undergo another procedure for coronary revascularization, then I came back and I could not get a cerebral protective device, but it's anecdotal. And if I can't do a cerebral protection, then I'm really going to say they need a carotid endarterectomy.

00:45:56

WILLIAM A. GRAY, MD: Yeah, I tend to agree with you guys both, and I like the approaches that you've all described here. We're not going to talk about flow reversal per se because we're in the sake of time, but you know, one thing that always happens, and I think the viewers are hearing is that there's a calculus that goes on during our procedure: as the thing becomes more complicated or more complex, the endarterectomy component or option becomes more prominent, and I think all of us as experienced operators have that clock running in our head in making sure we don't make the wrong decision for the patient. Because there is a good alternative. Let's move to the next video, please. And I would remind, as we're waiting for the next video, for our viewers to e-mail any questions that they have. We're going to have a spot at the end here where we can answer any questions that come in. So now you're going to see a pre-dilation with the -- with what is here a four-millimeter-diameter balloon by four-centimeter-length balloon. And that pre-dilation is meant to really create a pilot hole for the vessel -- in the vessel for the stent delivery system to be placed. And I think that it's -- you know, it's routine in our lab. We do it all the time. Here you can see the result of the pre-dilation. It actually looks pretty good even after what I would call an undersized balloon. And there are studies and there are advocates of not pre-dilating. I can't imagine not pre-dilating this particular lesion. Quick comments on whether or not pre-dilation is in your routine and whether or not you think that no pre-dilation actually offers any more safety or efficacy to the procedure.

00:47:24

JAMES F. McKINSEY, MD: I always pre-dilate every patient. I mean, I think this is something that it's safe, it's -- you're going to be dilating anyway, and worst case scenario, you don't want to have it where you put your stent and you can't get the stent-retracting device out, delivery system out because you just don't have enough room for the stent to expand. So it gives me an idea of the nature of the plaque, how easy it's going to dilate, how easy -- what size stent I should put in, everything else. One thing I do make a point of is that I always pre-dilate with a balloon that's shorter than the stent that I'm planning to use, because most of the time I want all the intervention done with angioplasty be done in a site that'll be covered by the stent, trying to decrease the risk of dissection. And same thing when I post-dilate, I dilate within the stent.

Pierre?

00:48:08

Y. PIERRE GOBIN, MD: I could not say that better. Just to add that I don't like to post-dilate when -- except when I have not a very good reason after the stent, but not only I like to pre-dilate, I like to dilate before the stent with -- size of a balloon -- with the final size of a balloon, the size that I want the artery to be. And then I will stent. And in many cases, I can avoid to post-dilate.

00:48:38

WILLIAM A. GRAY, MD: So you dilate with a five-millimeter balloon typically?

00:48:40

Y. PIERRE GOBIN, MD: I will -- before placing the stent, yeah.

00:48:43

WILLIAM A. GRAY, MD: You know, I'm in the same camp as you are and I think as Jim is, in that I don't -- especially in the symptomatic patient with a friable plaque, I don't really want to post-dilate that patient, because we know that that's where all the complications come from, especially with aggressive balloon sizing, and so if I can get away with a pre-dilation, a stent implant, and getting stuff out of there even with a residual 20-30% lesion, that'll be fine. And I think it sounds like we're in agreement on the panel. The next -- the next -- the next video, if you

could, is a stent deployment. And here you can see -- maybe you can't see it. I can hardly see it. The stent's going to come up here -- there you go. That stent's going to come up, the stent is 6-French compatible system. In this particular case it's a tapered stent, seven millimeters on the distal end, going to ten millimeters in the proximal end over four centimeters in length. And this particular stent will be deployed with a pull back of the sheath, exposing the nickel titanium, or Nitinol, material to the blood, which will cause it to expand in a thermoelastic way and apply to the vessel, because it's been oversized to that vessel. So here comes the stent deployment. A little more contrast, just to double-check, and then here comes the deployment. It's deploying from the top of the screen down. You see the two markers there; that tells us where the stent's ends are. The stent is now deployed, and we should be able to take out the device that it was delivered on. So I used a tapered stent here. Why don't we comment on tapered stents versus non-tapered stents, length of stent, and then closed-cell versus open-cell. Jim?

00:50:24

JAMES F. McKINSEY, MD: I like the tapered stents, I think, aesthetically, but I don't have any data whatsoever that says that's the right thing to do. I think -- you know, I get very get results with a non-tapered stent. What I try and look at when I'm -- one is the length of the stent I'm going to use, be looking at the area where the atherosclerotic plaque actually is, but also I'm looking at the curvature of the common carotid going into the internal carotid artery. And if it looks like I'm going to land and I'm going to have a kink or a hinge point right behind it, I'll -- we'll use a little longer stent or land a little bit lower, depending on what I can do, to try and maximize the positioning of the stent, even if I have to use a bit longer stent. The other thing is I always go into the common carotid artery. Even if it looks like an internal carotid lesion, I'll bring it down into the common carotid. I think the current stent technology, I prefer a closed-cell technique, but I think either one of them is working exceptionally well, and I need more data to tell me which is better.

00:51:22

Y. PIERRE GOBIN, MD: I agree with everything that you said.

00:51:24

WILLIAM A. GRAY, MD: Let's move on then to the next video clip. We'll come back to -- I know Jim has some slides on cell design, open-cell, closed-cell. We can talk about that then. And this is the -- this is going to be the post-deployment dilation. What you don't see here is the angiogram that showed us that we weren't quite done yet, and in asymptomatic patient, a 5-0 balloon is probably a reasonably safe thing to do and gives us a good caliber stent result. I tend to not go very high and I only do one inflation. As Jim mentioned earlier, we usual-- we try to use a balloon which is shorter than the stent itself so we stay inside the stent margins. In this case, it's a two-centimeter stent and a four-centimeter -- sorry, a two-centimeter balloon and four-centimeter stent. And you saw there momentarily a hemodynamic tracing, both blood pressure and pulse, and I think it's worthwhile commenting on, you know, both choice of size and pressure, but more importantly, management of hypotension/hypertension, post-procedural bradycardia and so on. Pierre?

00:52:26

Y. PIERRE GOBIN, MD: So first, what -- what pressure -- well, the minimal pressure necessary to expand the stent, as you say, is blood pressure that you want to apply. There is no reason to go much higher than the 6 atmosphere, sometimes 8 that are necessary just to reduce the stenosis. Another reason to stop, of course, is if your patient becomes bradycardic or hypotensive, sure, of course. That's a reason to stop, give atropine, and then if the stenosis has not disappeared, try

again. Then a very important question is management of a patient after the procedure. Those patients are probably atherosclerotic, so it means that they have also coronary disease. So you don't want them to be hypotensive and you don't want them to be hypertensive. So I -- our management is always done in the -- not on the floor, but in recovery, intensive-care type unit. Just for the tight management of his blood pressure. And these patients are doing well, so you say why do they need an intensive care unit? Well, I think they need an intensive care unit because statistically if you want 100% -- 100% of your patients to do well and not 90%, then this very tight control of the blood pressure is going to -- is going to give you better results.

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WILLIAM A. GRAY, MD: Yeah, I would agree. And I would love Jim's comments. I know that there is some data from the surgical literature that tells us that transcranial Doppler flows more than 150% of the baseline post-endarterectomy pres-- may present with an increased bleeding risk, and so we're pretty aggressive as well. Jim, how about you?

00:54:14

JAMES F. McKINSEY, MD: Yeah, I mean, we certainly are aggressive in watching peri-procedure, especially when the balloon goes up. I differ a little bit with Pierre in that I tend to use a small pre-dil balloon rather than the size I'm looking to get unless it's a symptomatic patient.

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Y. PIERRE GOBIN, MD: Sorry, I did not understand myself -- I will pre-angioplasty with a small balloon, three or four millimeter, and then do an angioplasty with a final balloon before the stent. I will not angioplasty from the scratch with a big balloon. I will use two balloons rather than one. So I do it progressively.

00:54:51

JAMES F. McKINSEY, MD: I see. Okay. I think that's a very similar technique, then. But one thing I do use is that smaller balloon to see what type of hemodynamic -- are they going to become bradycardic when I put the small balloon up? I tend to go up -- come down with a very quick inflation time. If they're bradycardic to start with, heart rate less than 70 or so, I tend to give a half an amp or half a milligram of atropine prophylactically once I'm sure they're adequate volume on board. So I mean, those are things that I look at pre-dilatation. Post, yes, I'm very aggressive looking at blood-pressure control. We'll look at hemodynamics such as their systolic and diastolic blood pressure, heart rate, and what their baseline blood pressure was. So if they came in, I try to keep them within about 10-15% of their baseline. If they're profoundly hypertensive coming in, I'll go more aggressive in lowering the pressure in that.

00:55:42

WILLIAM A. GRAY, MD: Okay, and then on the final angiogram we have keyed up here, we should see a final contrast injection and intracranial angiogram. And so let's go to that.

00:55:54

JAMES F. McKINSEY, MD: I think we have filter retrieval first.

00:55:55

WILLIAM A. GRAY, MD: Oh, I'm sorry, you're right. We have filter retrieval. Sounds good. Okay, so this is the embolic retrieval catheter. The catheter has to go through a stent. One of the reasons to post-dilate a stent is actually to lay down the stent's struts a little bit so this catheter can come through. You see the four prongs there now being recaptured into the embolic protection retrieval system. It's pulled out together with the filter. We usually back lead the guide or sheath so that we don't have any problems with captured material in the sheath being then injected into the cerebral circulation. And that's really the completion of the procedure. And

before I ask questions, let's take the final pictures, because I think we can combine those things. Can we go to the next video? So this is the completion angiogram. You know, this is a pretty good-looking result. You can see that the area of stenosis, which was 85-90% plus with reduced flow, is now fully expanded actually as much or more than it needs to be. Still, we don't see an A-1 segment here, but the middle cerebral artery segment I would submit not only is the flow but the blush is a bit better than we saw in the initial angiography. So at least qualitatively, it looks like better flow, even if we can't demonstrate that on an A-1 segment. So regards filter retrieval and final angiography, there may be some hang-ups on filters. You can get caught on the stent, you may have difficulty transiting the retrieval catheter in through the stent for a variety of different reasons, either on the edge or intrastent. And then you may even before you get there, when you take your initial test of contrast, you may see that there's slow flow. So there are different ideologies of slow flow. Jim, maybe you could talk to what the -- what you do in that situation. Pierre, you could speak to how you would treat a difficult filter.

00:57:43

JAMES F. McKINSEY, MD: I mean, I think that's one of the important things, that once you've completed your angioplasty and stent, everyone says, it's great, you know, let's call it a day, but you have to get these completion films. You have to look before you retrieve the filter of what's going on around the filter. If the filters worked and actually caught an embolus, the last thing you want to do is just pull it out. Sometimes there can be spasm in the normal carotid artery where you put the filter, which is also a concern. So if I see low flow and the patient's neurologically intact, I'll generally give a little nitroglycerin, 100 micrograms per cc, two or three cc's to see if that will help break the spasm. While I'm doing that, I'll be getting an aspiration catheter ready, because if I have slow or no flow I'm concerned that not only is there embolus within the filtering device, but there may be clot or embolus that are floating below that since we no longer have flow forcing it into the filter. So I'll bring an aspiration catheter up, come park it right below the filter, and aspirate that whole column of blood to make sure I'm not having any residual debris that's floating and as soon as I take the filter down that could be embolized to the brain. I will then repeat the angiogram and see if it hasn't improved. Majority of time, that does it. You've aspirated, you've given nitroglycerin, and you get brisk flow back. Then I'll retrieve the filtering device. If it still has low flow/no flow, then I have to certainly be concerned that I've got a major embolus in there. Then you have to figure out what you're going to do next, and that's something where I'll aspirate one more time. Eventually, you're going to have to recover that filter device. I've heard kind of going and putting a second filter up, but it just doesn't work well because something's going to go; as soon as you let that one filter down, it's going to go. That's the advantage of the reversal device, but in my mind and in my experience, I've never had that be a problem. Aspirate, get good flow, and then retrieve your device. Pierre?

00:59:30

WILLIAM A. GRAY, MD: Pierre, how about the difficult retrieval system? What do you do then?

00:59:34

Y. PIERRE GOBIN, MD: Usually this doesn't happen if you're -- if you are placing your stent or if your insert is good. If your stent is wide open, if there is no kink, it just should not happen. When this happens, then what you have to do is to change -- change the anatomy. And you know, those vessels, I mean, the internal carotid artery is really mobile, so you can change the anatomy. To change the anatomy, you can ask the patient to take some deep breaths and stay in extreme inspiration or in extreme expiration, and then the position of the carotid artery will

change, and then we can try to pull again. And another trick is to ask the patient to cough when you pull, and this may work. Finally, a final trick is to just take your gloves of one hand off and press carefully slightly on the carotid artery and try to modify the curves while -- with your left hand while with the right hand you pull the filter. And with all of those tricks, it's really well that you cannot get the filter back. It doesn't happen to me.

01:00:42

WILLIAM A. GRAY, MD: In addition to those, I've used all those and I've used a couple things that aren't so routine. Many times a patient will have -- had pillows put under their head or a basket to hold their head; we take those out and let their head recline, and that actually changes the angle when we turn them right and left. And the one that really works very well and actually has gotten me out of a lot of trouble is just to have them swallow. And if you time it just right, the swallow changes so much of the carotid anatomy that you can actually usually get your filter system out.

01:01:09

Y. PIERRE GOBIN, MD: I wonder, also -- I've never tried it -- but maybe placing your buddy wire can potentially help.

01:01:15

WILLIAM A. GRAY, MD: Sure, yeah. Enough to do it. And sometimes you can change the aspect or the bias of the filter wire by pushing it up against the petrous segment; you can actually bounce the filter wire and bow it off the -- off of the stent to lessen that curve. So we need to move into our final aspect, which is our clinical trial data sets. We want to speak briefly about SAPPHIRE, CAPTURE, CREST, and EVA3S. Each of them are relevant and important. Let's go first to the next slide. The next slide really talks about the SAPPHIRE data set as it relates to cases in SAPPHIRE worldwide. SAPPHIRE worldwide and CASES are the aftermarket or post-market approval trials, and SAPPHIRE was the granddaddy trial that really helped get these devices approved in the U.S. And you can see here, with the different colors both in the individual endpoints as well as the composite endpoint of stroke and death or stroke, death, and MI, which is that MAE last on the right endpoint, that there are really no differences between the pivotal trial and the trials that followed on after approval, which is an important component of moving any technology from a clinical trial setting into a real-world, if you will, or the clinical environment.

01:02:27

JAMES F. MCKINSEY, MD: So, Bill, you're seeing about a 4-5% major adverse event at 30 days and -- from the beginning into these trials.

01:02:36

WILLIAM A. GRAY, MD: Exactly. And we'll have another trial slide here in a moment about what that looks like across trials. One of the other issues that we haven't really talked about here but we all know is that when you put a carotid stent in, the major thing that we've talked about here is doing it safely. Because doing it safely basically determines the patient's long-term risk, and you can see in the SAPPHIRE trial that the difference between endarterectomy and stenting out to three years -- this was just recently published in *The New England Journal of Medicine* -- showed no significant differences in the outcome of stroke as it relates to either procedure, endarterectomy or stenting. And you know, that wasn't a given when we started stenting, but clearly it is an effective stroke preventative. Next slide. And this is just a combination of seven different trials which were pivotal trials looking at basically filter embolic protection. One of them, the NASCET trial, had a -- had a balloon occlusion, but the bottom line is that all the trials

came in almost equivalently in terms of their outcomes. The major adverse outcome rate, as Jim mentioned, is about 5-6% and it compares favorably to the contemporary control of SAPPHERE endarterectomy, which was about 12.5%. So all in all, I think a pretty good experience in the pre-market approval. We'll look momentarily here at a post-market, but we want to talk a little bit about where strokes occur in cryostenting. This is an analysis of a CAPTURE 3500 cohort which was recently published last winter and showed that not all strokes occur in the areas where we're working. About 20%, which is fully 1% of the absolute stroke rates, are occurring in the contralateral or nonipsilateral hemisphere. Most of those strokes are minor, but it speaks to the issue of access and whether or not we can do better on access. We talked a little bit about our selection of both access points and access techniques. Next slide. We can go to the next slide, I think, because this highlights the same point. And then, you know, this is a slide which basically shows that since approval in 2004 with the -- with the temporal rollout of these different trials, first CAPTURE, CAPTURE 2, EXACT, and CASES and SAPPHERE worldwide and others, that we've seen an increasing safety margin compared to the pivotal trials that got these devices approved. So you know, we're seeing a rapid improvement in outcomes even in these high-risk patients, which I think is gratifying for everybody involved. We will see the next wave, both with the MoMA device and the Gore Parodi device, flow reversal in this country. And we'll see outcomes there. They don't differ, at least at this point, from the European data sets with the U.S. data sets in carotid stenting with filters. Next. Pierre.

01:05:11

Y. PIERRE GOBIN, MD: So CREST is a very, very important trial, a prospective randomized multicenter trial that compared carotid artery stenting with carotid endarterectomy. 2,500 participants -- patients were enrolled, and the trial is actually completed. As of July 10, 2008, 2,516 were enrolled. The primary endpoint of CREST was -- was how well carotid artery stenting and carotid endarterectomy can prevent stroke and death during the 30 days after the procedure or the ipsilateral risk of stroke at one year. Next. Each physician doing a carotid stenting in stroke had to have 20 leading cases. Next. And then a patient -- then a physician could randomize patients as I just tell you, their randomization phase is finished. What the leading phase results are telling us is that overall, 30-day of risk of death or stroke was 4.6%. In symptomatic patients, this risk was 6.5%. And we can already identify some subgroup that shows that, as kind of expected, carotid stenting is a little more risky in diabetic patients and it's more risky in older patients. This we don't know if it's just because of age or if because the anatomy was more difficult, because I must say that in my experience I don't have a higher risk of complication in old patients, so maybe it's just -- shows the anatomy in a selection of patients. Next. EVA3S was a trial performed in France randomizing patients, carotid artery stenting versus carotid endarterectomy in 40 centers. And the trial was stopped early for reasons of safety and futility. Next. Because the trial showed that carotid artery -- carotid endarterectomy was actually safer than carotid stenting, at least in this population of patients. And the risk of cerebral vascular -- cerebral vascular event or death at 30 days was 3.9% after carotid endarterectomy versus 9.6% after carotid stenting. Next. And there were some problems about EVA3S because the rate of stroke complication after carotid stenting in EVA3S is so much higher than what we have in the U.S. that we think that this was mostly to the fact that interventionalists that were enrolling patients -- that were performing carotid stenting in EVA3S did not have enough experience and they were working with devices that they did not -- that they had no experience with before. And maybe three was also an issue in patient selection. Next.

01:08:30

JAMES F. McKINSEY, MD: So, Bill, perhaps you can comment on where we see carotid stenting going.

01:08:34

WILLIAM A. GRAY, MD: Yeah, I think the next phase of carotid stenting really is in a couple of different fashions. One is in the patient who has good risk for surgery, both symptomatic and asymptomatic, which is what CREST just -- Pierre just outlined, CREST will help to give us information about. Secondly, we have small sets of data that talk about the 50-70% stenosis in the symptomatic patient, which we know in surgery from the NASCET trial, although less robust in terms of its benefit, still did benefit patients. We don't know that as well in carotid stenting. And then lastly, you know, what to do with the aged patient. As Jim will outline here momentarily, at Columbia we don't see this age differential in many other individual and some multicenter expert sites, we don't see this age differential. So it seems like it may be selection of patient and/or operator skills, but we don't really have that answer. It's all speculative. Next slide. As Pierre said, the standard surgical risk trials in asymptomatic patients are basically coming down the home stretch. We've got the CREST trial finish last week, ACT 1, which is another trial looking only at asymptomatic patients, is about a third of the way finished. And I believe with CREST completion, we should see that bump up pretty quickly. And this was a time course predictor actually written about two years ago and right on target: July 2008 we finish the trial. Lastly, post-procedural management, and then I'll turn this back over to Jim for our NYP outcomes. Post-procedure, patients will stay on aspirin and Plavix for 30 days and then aspirin for life, as any atherosclerotic patient might. Follow-up is typically a 30-day follow-up for both neurologic evaluation and then some duplex evaluation in the first 30 days or six months. And then six months and twelve months, duplex evaluation, at least in our office, or at least in our practice. And then lastly, we take -- take carotid -- sorry, coronary and atherosclerotic risk factor prevention, which would include blood pressure control, statin therapy, and things that Jim outlined at the beginning as potential therapies broadly for the vascular patient. So, Jim, do you want to talk to us about the NYP experience in carotid stenting the last few years?

01:10:46

JAMES F. McKINSEY, MD: Yeah, I think this is something that we really outlined over the last hour of what can be done with carotid stenting, but the really important thing to our viewers and to us as practitioners: what are our own results? I mean, if we're saying this is what the NASCET is getting but we're not meeting those standards or, preferably, beating them, then we're doing the wrong thing. So we've actually gone back and looked at the NYP experience, which is a multidisciplinary program which we have a separate coordinator that actually looks at our data and helps coordinate the outcomes and allows us to put these reports together. So it's more of an unbiased report. The multidisciplinary group consists of vascular surgery, the interventional neuroradiologists, the interventional cardiology group, as well as interventional neurosurgery. So again, we have the ability to really look and discuss among ourselves or to ourselves what's the best procedure to be done for any individual patient so that if it's better they have carotid endarterectomy, certainly we can supply that. If it's better for carotid stenting, we have very capable people of doing that. As I mentioned, it's all entered into an independent database that was originally created by the Society for Vascular Surgery that monitors the registry and our outcomes. As we look at it, we had 298 patients that were enrolled in the carotid stent angioplasty registry between May 5th of 2005 and September 30th of 2007. There was 168 patients that were without symptoms but with stenosis greater than 80%, and there was 130 patients -- or 43% -- that were symptomatic. We had a 30-day follow-up in 94% of the patients.

We had very good follow-up looking at the outcomes. What we found is that if we look at stroke and death -- this is all stroke and death -- we had a 1.2% incidence at 30 days. So if we look at the national trials that we just outlined, that's well below the 4-5% that's being reported nationally. If you look at the asymptomatic patient, that number's even lower at 0.6% and slightly higher for the symptomatic patient at 2.4%. If we look at stroke death and myocardial infarction -- as Bill alluded to, coronary disease is always a concern with patients with carotid artery disease -- we see that if we look at stroke, death, and MI, that number goes up to about 1.9%. Again, markedly below the national average and in these national trials. Asymptomatic still doing better at 1.2% compared to the symptomatic patient at 3.2%. If we look at any neurologic deficit -- Dr. Gobin indicated that there can be a contralateral, or the opposite side, stroke during some of these procedures as well as death and myocardial infarction -- and we're at a 3.5% 30-day stroke, death, and any neurologic event. These also include -- and actually the majority of these are patients that have a transient event -- a little bit of weakness, a little bit of confusion -- that completely clears within 24 hours, but we certainly for the sake of completeness did include it, so even TIAs were included in our study, giving us a global rate of 3.5%. But the main point is our stroke and death rate, the major sequelae of this procedure, is exceptionally low at 1.2%. So in conclusion, I think carotid artery stenting is a good option for patients that are at risk for carotid surgery. Carotid artery stenting outcomes are dependent on the expertise of the operators and the institution, and I think we just showed that the collaborative effort at New York-Presbyterian Hospital System has resulted in exceptional outcomes for our patient population. And the current study results are pending, which will determine the role of carotid stenting in the healthier patients, the non-high-risk and the asymptomatic patient population. So we have received some questions from our listeners, so I'd like to put the first one to Dr. Gobin: what are your thoughts on endosurgical stenting and angioplasty using neural protection, filter neural protection, to repair a cervical internal to external carotid artery anastomotic stenosis? A pretty complex question here, Pierre.

01:14:48

Y. PIERRE GOBIN, MD: Yeah, it's a complex question because it's a complex procedure. I suppose that this is a case of a patient who had a carotid occlusion and a neurosurgeon constructed a bypass from the external carotid artery and typically the temporal artery to the intracranial circulation, and this bypass has stenosed. So it's certainly a much more complex problem than just performing the plain carotid artery stenting. What we'll have to analyze is first, does the patient need this bypass? Is he still symptomatic? Because the patient may have needed a bypass at the time and then after several years, the need for the bypass may decrease. Then if the stenosis is there, where is it? Is it at the origin of the bypass? Is it low in the neck where the external carotid artery takes off? Because if this is the case and if it is symptomatic, then it is easy to perform just a simple balloon angioplasty. While if the bypass -- I mean, if the stenosis is at the distal anastomosis of the intracranial anastomosis, then the angioplasty is still possible, but it's certainly significantly more risky and it -- the indication will depend on the anatomy and of the symptoms. So it's a complex -- it's a complex case.

01:16:09

JAMES F. MCKINSEY, MD: Certainly. And we have time for just a couple questions, so I'm going to take the next question and put it to Dr. Gray. You know, one thing we've seen in the trials and one of the advantages with carotid stenting is that especially redo carotid surgery, there is an incidence of cranial nerve injury. It may be transient, it could be permanent, certainly, because you're dissecting and operating in that field. But what we've noticed also, and in the

national trials, there is a very small but not zero reported incidence of cranial nerve injury. And so the question from one of our listeners is how can we rectify or justify a cranial nerve injury with carotid stenting? And the other question is what is the incidence and the potential for intercranial bleeding with carotid stent? Bill?

01:16:54

WILLIAM A. GRAY, MD: Both interesting questions and occur at such a low incidence that it's difficult to make any definitive statements about them, but the only data I'm really aware of in a randomized multicenter trial that talks about a dissection and/or cranial nerve injury is in the EVA3S trial. And 5% of those patients actually went to surgery. And I looked back at the pivotal trials in the U.S. -- the SAPPHIRE, the ARChERs, and so on -- and found that no patient went to emergency surgery. So I think it speaks a little bit to the issues that Pierre was raising about whether or not these patients -- or these doctors -- were really fully qualified to do this procedure, since we're not seeing that. I've never seen it in my 13 years of doing this procedure that patients have actually had a cranial nerve injury. Now, occasionally they'll have a cough when we blow up the balloon. That reflex is not well understood. But it's not a permanent one. The other things you might wonder about are persistent hypotension, which does occasionally occur, but usually after a day or two of ambulation it gets better. Or bradycardia, leading to pacemaker requirements. And I've seen that only once, and it probably was incidental to the patient's age and conduction system abnormality. So it turns out from a neuro-- from a local neurologic standpoint that palsy is rare if it ever happens. And so I don't really have to rectify that much. As far as the intracranial bleed, that does occur, as Pierre mentioned several times through this broadcast. I think the issues there largely have to do with isolated territory, symptomatic patients, the elderly, poor perfusion, tight lesions. And tight blood pressure control, not hyper-aggressive anticoagulation or antiplatelet therapies, like not giving TB3 inhibitors and so on I think are really important components of those patients. And for those patients who are -- who can delay or defer a hemodynamic stenosis, if we can stabilize them out a few weeks for -- to let them become let symptomatic, let the blood brain barrier reestablish itself, we try to do that. But sometimes you don't have much of a choice. The incidence is less than half a percent, and I think actually less in the filter embolic protection era.

01:18:57

JAMES F. McKINSEY, MD: I think that's true and then we all saw that for carotid. Well, I think our final question is one to conclude on, and this is: regarding stroke prevention, how do you diagnose patients that have potential problems with their carotids? And I think this is something that's important for all physicians to look at. If you have a patient that has any neurologic symptom, certainly that needs to be investigated. If you're not comfortable, certainly a referral to a carotid expert as on the panel today or a neurologist to further evaluate that. A good physical exam, listening to the neck arteries for signs of turbulent flow, or what we call bruits, which will help alert you that there's ongoing atherosclerotic disease. And quite candidly, people with coronary artery disease, as Bill and I have talked about frequently, are ones also subjected to a potential for carotid disease, and they should be screened. And this is where we need to also look forward for our government and Medicare of how we're actually going to start screening patients to try and help detect this potential treatable lesion that could have a devastating complication, its first symptom being a stroke. So with that, we'll conclude tonight. I'd like to thank both Bill and Pierre for their time and we thank you for joining us tonight. Good night.

01:20:07

Y. PIERRE GOBIN, MD: Thank you, good night.

WILLIAM A. GRAY, MD: Good night.

01:20:12

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