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Peripheral Arterial Disease (PAD): Revascularization for Clinical Limb Ischemia

Dr. Caudle:
This is ReachMD and I'm your host, Dr. Jennifer Caudle, and joining me today is Dr. Timothy Clark, Associate Professor of Clinical Radiology and the Director of Interventional Radiology at Penn Presbyterian Medical Center. We will be discussing the diagnosis, management, and treatment of peripheral arterial disease. We will also be discussing the revascularization for clinical limb ischemia. Dr. Clark, welcome to the program.

Dr. Clark:
Thank you. Glad to be able to join you today.

Dr. Caudle:
So, let's start out. Can you tell us about how common peripheral arterial disease is in the United States?

Dr. Clark:
Well, it's extraordinarily common and currently affects somewhere around 12 million Americans. Those estimates have been as high as 15 million people in this country, but what's interesting is the number of people who have it, the prevalence of people who have it, is continuing to grow and grow as some of the chronic health conditions that are catching up with people, particularly people over the age of 60 to 65, start to take their effect. So, diabetes, hypertension, out national obesity epidemic, dietary things, and then some well-known risk factors for peripheral arterial disease that we're all aware of, so smoking, high cholesterol, a strong family history. So there's a lot of people out there and what's especially interesting is, looking at the proportion of those 12 to 15 million people, it's only a very small subset, it's about 5% of those people actually have their PAD, peripheral arterial disease, diagnosed and appropriately managed.

Dr. Caudle:
Can you talk about what the main risk factors for peripheral arterial disease are?

Dr. Clark:
Well, that's a great question. Certainly the biggest factors would be smoking, and even former smokers who have long since quit will still harbor that risk for the development of peripheral arterial disease. Diabetes is also a huge risk factor. The longer you've have had diabetes and the diabetic control that a diabetic may have, is also very, very influential into how likely a person is to develop peripheral arterial disease, and then, your lipids. So, hypercholesterolemia is another independent risk factor for peripheral arterial disease. And then, a family history. So those four together are sort of considered the four biggest risk factors for PAD.

Dr. Caudle:
How is peripheral arterial disease diagnosed and managed?

Dr. Clark:
Well, it's diagnosis can be rather elusive because when a patient comes into the office for another complaint, or even one related to PAD, it's oftentimes some of the fundamental screening tests that can be very helpful for diagnosing PAD may not be available or may not be done. And that, I'm talking about the ankle brachial index, which is the ratio of usually the systolic blood pressure between the brachial artery and each ankle. And so, the other thing is that a symptomatic patient, unless they're exercising, unless they just climbed 6 flights of stairs to get up to your office, they may walk in and have a normal or nearly-normal ABI, so that even if an ABI is performed during an office visit and the feet are checked for pedal pulses, capillary refill, trophic changes, thickening of the toenails, sparse hair below the knees, the other sort of common physical signs of symptomatic PAD, those can be missed. Really, I think, if there was 1

simple office assessment to diagnose the presence of peripheral arterial disease, it's one of the oldest cardinal signs, but it's still the most helpful in a lot of those patients, and that is elevating the patient's extremity while they're lying down, allowing the blood to kind of leave their leg, and watching for the development of pallor of their foot and lower leg. And then, lowering the leg after about 30 seconds, allowing it to dangle below the examination table several inches, and then looking for it to redden and become ruborous. So that combination, so-called pallor-with-elevation and rubor-with-dependency is, when we teach people how to evaluate patients for PAD, that is one of the most consistent physical signs that you can elicit in the office. And a lot of folks who will have, especially diabetic people, they can have noncompressible tibial vessels and so an ankle brachial index may be spuriously elevated. We'll see patients with advanced stages of peripheral arterial disease where they're facing limb loss from impending or active gangrene and they may have nearly normal or even a supernormal ankle brachial index, because you simply can't compress those calcified tibial vessels. So pallor-with-elevation and rubor-with-dependency is an incredibly helpful physical sign. Once the history and physical points towards peripheral arterial disease, it becomes a matter of trying to control as many of the risk factors as possible, so that's smoking cessation, lipid control, exercise certainly helps, and then making sure blood pressure is well controlled. Most patients are also going to be on a statin as well and there's a lot of evidence that statins will help to certainly slow the progression of PAD and may even allow some PAD symptoms to respond over time. Certainly the administration of statins at the time of vascular procedures, both open bypass surgery and minimally invasive endovascular procedures, statins have been shown that, if they're administered in the perioperative or periprocedure period, that that can reduce complications occurring in that interval of time.

Dr. Caudle:
That's very helpful. If you're just tuning in, you're listening to Medical Breakthroughs from Penn Medicine on ReachMD. I'm your host, Dr. Jennifer Caudle, and Dr. Timothy Clark, Associate Professor of Clinical Radiology and the Director of Interventional Radiology at Penn Presbyterian Medical Center is joining me today.

So, can you talk to me a little bit about what the role of endovascular therapy is in symptomatic peripheral arterial disease patients?

Dr. Clark:
Well, it's been a paradigm that's undergone quite a series of dramatic changes. In the last 10 to 15 years, there's been a marked reversal in the role of endovascular therapy for patients with symptomatic peripheral arterial disease. So these are patients who have lifestyle disabling claudication or they've advanced to rest pain, or they've been developing tissue loss. When I first trained as a Fellow at Penn, about 80% of patients who had symptomatic peripheral arterial disease, who were suitable candidates for an intervention, they would undergo bypass surgery and only the subset of about 20% who were deemed to be too high risk for surgery would undergo endovascular procedures. Today, as of 2016, it's now completely flip-flopped so that the endovascular-first strategy is considered the way to go for most patients. It's got a shorter recovery time, it's got fewer risks. So, reduced morbidity, reduced mortality, probably reduced cost, and if it's done properly, it does not deprive patients of other bypass options in the future should they develop problems down the road that are not fixable with endovascular therapy. So currently, about 80% of procedures are done endovascularly and open surgery is really reserved for those who have had endovascular therapy and have developed a problem where endovascular procedures cannot salvage the problem that's developed, or patients who prefer an open surgical approach. As we know, most people would prefer a less-invasive approach.

Dr. Caudle:
Great. Can you talk about what are some of the common endovascular procedures for peripheral arterial disease?

Dr. Clark:
Well, the most established is percutaneous angioplasty and that's been something that first came into medical use 50 years ago in the form of threading progressively larger dilators across a stenotic lesion to increase blood flow through a stenotic segment of an artery, followed several years later by the development of a balloon catheter that could be inflated and then deflated and removed at the site of an atherosclerotic stenosis. Certainly angioplasty is something we continue to have as our mainstay endovascular therapy. Stents are something that we're all familiar with. They act as a scaffold that holds the artery open in a more permanent fashion than does a balloon, and they can act as a matrix for a new intimal lining, a so-called neointima. But stent technology has come a huge way in terms of the technological advances over the last 15 years or so and those changes continue to make huge strides. For example, we've had stents that used to be so large you required massive introducer sheaths in order to be able to insert them into an artery. We now have stents that can go through delivery system that's as small as 4 Fr. A 4 Fr. sheath is something that is a little more than about a couple of mm in diameter. In fact, some of these are so small they can be inserted through a vessel in the foot or through the radial artery or ulnar artery near the wrist, incredible miniaturization of stent technology. We're all familiar with drug-eluting stents and the drug-eluting stents are those that are coated with agents that can reduce the proliferative response that occurs at the site of stent placement, so the hyperplasia, fiberglass, and smooth muscle cells that can lead to in-stent restenosis, well that can often be managed upfront at the time of stent placement by choosing a device that contains basically an anti-proliferative agent that is going to block or reduce that effect.

And the delivery mechanism for those, the polymers, the coatings that ensure a controlled release of the agent at the right dose level, there's been great advances made in that just in the last few years and those technologies continue to be refined. But what we're particularly excited about in the endovascular world are the dissolvable stents where you can repair the vessel endovascularly by putting in a stent and get the immediate effect of restoring blood flow, but over time the stent dissolves and leaves nothing behind and the vessel is, you know, the stenosis has been fixed, but there's no permanent implant left behind and that can be very advantageous for a number of reasons. That means you've got an artery that doesn't have a piece of metal in it and metal can ultimately fatigue and fracture in certain anatomic locations in the body. So that can be an advantage. And the biomaterials that are used for creating an absorbable stent can be combined with the same drugs that we're now seeing on the drug-eluting metal stents. So you can have a stent that, first of all, will dissolve over 18 months or so after implantation, but during the first few weeks to months after implantation, will absorb out a drug like one of the Limus family drugs or paclitaxel, or a combination of drugs, that is going to limit or reduce the level of intimal hyperplasia.

Dr. Caudle:
That's fantastic. You mentioned a number of different procedures. Are there examples of some additional or newer advanced therapies that you would also like to mention that have made a difference in some of your patients?

Dr. Clark:
Well, that's a great question, Dr. Caudle. Absolutely there are other very exciting technologies that have become available and we, as interventionalists, as we gain more and more experience with these technologies and as the technologies themselves become more refined, it's really extended the spectrum of people whom we can help. We've had patients where, 10 years ago, there would be no way we could save somebody's leg. The level of ischemia would be too far advanced, they wouldn't have any autologous vein for a vein bypass, they wouldn't be candidates for a synthetic bypass graft, they wouldn't be candidates for anything endovascular, and so really, their only fate would be that of amputation. Now, the available technologies we have, in terms of smaller devices, devices that can go through blockages much more readily, has really just exploded. One of the things I've had a particular clinical interest in is basically performing internal bypasses, meaning having a patient with a completely blocked artery, what we often term a chronic total occlusion, an artery that may have been blocked for months, years, even decades, and the patient having symptoms, oft times severe symptoms, as a result. In the past, these patients were felt to be untreatable by anything other than surgical bypass, but over the last decade, and especially in the last 5 or 6 years, a whole series of techniques and dedicated devices to serve those techniques have evolved where we can actually create a new channel inside the wall of the chronically-blocked artery and open up that channel with balloons and stents to internally bypass blood around the obstructed artery. It's really nothing short of extraordinary. I mean, to be able to take a patient who would have been looking at a large scar running right from their groin all the way down to below their knee, several days in the hospital, which would be typical of somebody with the old way of doing it, a fem-pop bypass, having somebody like that where we can actually go in, do the same thing, provide a complete bypass of the obstructed artery, and do it and have them go home the same day or early the next morning with just a Band-Aid over the little nick that we went in, is really extraordinary. So, so, yes, the devices that we have for crossing these chronically-obstructed arteries and getting beyond the diseased segment of the artery and then getting back into the healthy part of the artery and then creating that shunt through the wall of the vessel, that's been very exciting.

The other thing that we're seeing a large series of developments in has been that of the ways by which we can remove plaque from inside the artery. So, there are technologies that allow us to vaporize away the plaque with lasers, with a technique called photoablation where an Excimer laser is on the end of a catheter and that is brought up to where the area of the plaque is and the laser is activated and the plaque is literally evaporated. Other things that we can do are to use specialty catheters that shave away areas of plaque and this can be done in a very controlled fashion allowing us to shave out the plaque and leave the healthy part of the artery behind. That's been another big development. And there are ways in which we can modify plaque by taking a small burr that essentially sands away the plaque, that does so by sanding it into particles that are so small that they're cleared away in the bloodstream without blocking the smaller arteries downstream of where we're working. So, that's been a huge advantage for a number of our patients where really we've felt that those kinds of technologies have made the difference between success, that is, getting enough blood restored to the patient's leg that they're not going to have an amputation, and lack of success where we might not have been able to do that.

Dr. Caudle:
Well you know, and my final question is sort of an extension of some of the therapies that you talked about, what do you see as promising future endovascular therapies for peripheral arterial disease?

Dr. Clark:
I think some of the extensions of what we're already doing now. We're now able to thread a catheter, for example, all the way down into a person's foot, if necessary, and track along with that catheter tiny balloons. We're able to angioplast the arteries open down right into the foot. That would be a territory we could never get before because it was too small. So, I think some of our existing technologies will

continue to become sort of micro-sized and allow us to get further and deeper into certain vascular territories when it's needed, to be able to get the level of local perfusion improved.

Our ability to measure blood flow in people's legs is also something that's been indirect so far. We can look at things like CTA and MRA, pulse volume recordings, impedance plethysmography and so forth, but all of these are essentially just looking at pressures and vessel caliber. They're not telling us how much is a person's calf muscle being perfused, how well is a person's skin at their foot being perfused? So some of the imaging technologies that are coming under development, I think, are going to hold a lot of promise in our ability to detect how much a person is at risk for limb loss from advanced peripheral arterial disease, and how best to treat those patients. So that's another exciting thing that we're looking forward to, and then, as I mentioned earlier, some of these bioabsorbable scaffolds, these stents that we can put into the body and allow them to remain there for the length of time they need for the artery to heal after we've opened up a blockage that then later dissolve away so that nothing is left behind, and we're expecting to see some great things come from those technologies in the next several years.

Dr. Caudle:
Dr. Clark, thank you so much for joining us today and sharing your insights on peripheral arterial disease.

Dr. Clark:
Well, thank you, Dr. Caudle. It's been a pleasure.

Dr. Caudle:
I am your host, Dr. Jennifer Caudle, and thank you for listening.