- So, hi everyone. My name is Anahita Dua. I am a vascular surgeon at the Massachusetts General Hospital, and an assistant professor of surgery at Harvard Medical School. I'm the co-director of our Peripheral Artery Disease Centre, associate director of our Wound Care Centre, director of our vascular lab, and director of clinical research in our vascular division. I'm so excited to talk to you today about a study that I was the national PI for, called the CLariTI study. Which essentially is a study focused on the natural progression of critical limb ischemia in the population across the United States, in order to provide some real-world data about what amputation rates are across the US.

Aims

The aim of this trial was to see what number of patients basically go on to get amputated, who are told that they're going to be amputated in the US. Essentially, the United States has a number of different providers that are involved in the care of a patient who has critical limb ischemia. Interventional radiologists, interventional cardiologists, general surgeons, vascular surgeons. And different parts of the US have different access to healthcare. And so as a result, we are not sure, there are basically no metrics out there, that tell us that in the United States what is the acceptable or normal amputation rate? Does it vary from location to location? Does it vary from specialty to specialty? Finding out that standardisation in the metrics, essentially is the first step in being able to combat the disease and decrease amputation rates. You can't decrease a rate that you don't know. And so, the point of this study was to essentially collect prospectively, in an observational fashion, 200 patients that had critical limb ischemia from across the US, and just follow them to see how many patients who were told they were going to get an amputation, did go on to get an amputation within a year.

Inclusion/Exclusion Criteria

So primarily, we included patients that had had two failed revascularization attempts, or a patient that was deemed to have no distal target to do a revascularization. What's interesting about that, is that can vary from provider to provider. So for example, at Mass General, if I see a patient and I think, "Well, yes, there's a distal target, "I could do a bypass on that." Maybe a provider in Missouri, for example, might think, "Oh no, this is not possible for this patient." And might go straight to amputation. And that inclusion, exclusion criteria was purposeful, because we wanted to see the variation in care that patients were getting across the US, based on the gestalt and the skills of the provider providing the care. So essentially again, a prospective observational study.

Study Design

We went across the United States and included any patient that had critical limb ischemia. And this was determined by either rest pain or tissue loss, primarily tissue loss. And again, inclusion criteria were patients that had undergone two revascularization attempts that had failed, or for patients that were deemed that they were not candidates for revascularization, because they had no distal target. We then followed out these patients for up to a year. And the study that we presented at LINC is essentially the interim results. So just up to three months, 'cause we're still very much in the process of following the patients.

Main Outcomes

At this point, we have closed the trial, we did make our numbers, but now we have a few more months to get the whole one year data, to see how these patients ultimately fare. So thus far, we've found that 33% of patients that are deemed non-revascularizable and told that they're going to need an amputation, have an amputation by the three month mark. We expect that number of course, to increase over the course of the next nine months to get us to the 12. And our main outcome essentially, was amputation-free survival, and, of course, amputation itself. We did note that there was a decent number of patients that exited the study because they did die. We had 200 patients as mentioned, and already by the three month mark, 26 of them either have been amputated or have died. And so, we of course have that group out, and then we see how many are left to progress through to the 12 month mark. So at this point, mortality is what we're looking at in conjunction with amputation. And again, 33% by three months already amputated.

Conclusions Regarding CLTI

Ah, that's the magic question. Thank you for asking. So basically, as I mentioned earlier, without knowing who your enemy is, you can't fight. So without knowing the metrics around amputation, we can't reduce amputation rates, because what is the rate? And so, the point of this study was to get that number. How many patients who have critical limb ischemia are being amputated, because they're deemed not revascularizable, because there's no target or they've indeed failed it? So there's a new technology on the scene. Deep venous arterialization essentially is a way in which we can take oxygenated blood and shunt it through the venous system to get down into the patient's foot. A lot of these patients, the reason that you can't revascularize them, is because they don't have arterial flow to the toes. But this new technology has shown a lot of promise, and, in fact, that's the name of the trial, the PROMISE trial, where they actually are looking at deep venous arterialization as a way in which to salvage legs of patients that are considered, quote, no option, there's no other option, but amputation. So what is going to be really impactful is once we know how many of these patients were amputated, we're going to go back and look at their angiograms, and we're going to determine how many of these patients, based on their angiographic anatomic data, would be candidates for deep venous arterialization. And how many of those patients, had they undergone deep venous arterialization, would have had their limbs salvaged. So ultimately the point of this trial, is to have the baseline statistics to know when we do have this new technology that's going to ideally be readily available in the next year or so, is it going to decrease amputation rates, because we're going to be able to offer these patients deep venous arterialization? The other really cool thing about this study is this was real-world data. Unfortunately, in the PAD world, there's a significant lack of diversity in our patient population, we don't have enough women, we don't have enough people of colour. And unfortunately, those two groups make up a lot of the patients that are getting amputated. This study is wonderful in that up to 30% of our patient population is African American or African, for example. So we're going to be able to do some subgroup analysis to figure out, is there anything else that we can shake out that we can go ahead and impact, in order to decrease amputation rates? So we have an opportunity with a wealth of observational data to do a a multitude of subgroup analyses and different disease processes, in different things like race, gender, and drugs, other things that potentially impact the amputation world. And simultaneously, are going to be able to see how many patients potentially would've been saved by deep venous arterialization, to allow that to ideally burst on the scene as an option for these no option patients.

Further Research Required

So the next step will be of course, to finish up the trial. We got to get to the 12 month mark and see what the numbers are at that point. After that, it's all about the statistical analysis. So after that, we're going to analyse the data in subgroups, specifically looking at comorbidities, race, gender, as I mentioned, and of course patient outcomes. And the other really important thing is the anatomy. You know, a patient that has tibial disease in the AT and the PT, may be a different patient than a patient that has tibial disease in the perineal and the PT, and how that impacts the patient in conjunction with the wound location, for example, is really important. Figuring out some of those nuances is really the next step, after doing this large real-world study.