At the 5th Annual Amputation Prevention Symposium in Chicago, Larry J. Diaz-Sandoval, MD, presented information on a study of CO₂ angiography conducted on critical limb ischemia patients with diabetes and chronic kidney disease. Vascular Disease Management spoke with Dr. Diaz about the study.

**VDM:** Tell us about how the study you conducted came about.

**Diaz:** About a year ago, I got in touch with Mariano Palena, MD, from the Foot and Ankle Clinic of the Policlinico Abano Terme in Padova, Italy, and we started talking about issues with patients with critical limb ischemia (CLI) and diabetes and how frequently they have advanced kidney disease. As we know, patients with CLI have multilevel and multivessel disease, which means that they are, generally speaking, going to require not one but several procedures in one leg to actually obtain full revascularization and avoid amputations. So far what has been done traditionally is these patients undergo procedures with the use of iodinated contrast media, which produces contrast-induced nephropathy, so for this patient that’s kind of like a catch-22 and in many cases unfortunately leads some of the doctors involved in their care to tell them, “I really don’t know that you should go with this procedure because you’re going to lose your kidneys.” That continues to be a fear, and we are trying to show people that is not necessarily the case. We have technology and we have techniques nowadays that can overcome this.

One of these newer techniques is carbon dioxide or CO₂ angiography. Some operators prefer not to use CO₂ because there is some degradation of the image quality as you move downward in the arterial tree, especially when you get to areas of chronic total occlusion because of the high diffusion capacity of CO₂, which goes very rapidly in small capillaries and collaterals that are typically located at areas where you have total occlusions. That probably used to be very frequently

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**Dr. Diaz** is an interventional cardiologist at Metro Health Hospital in Wyoming, Michigan, and faculty member of the Amputation Prevention Symposium. Dr. Diaz reports no disclosures related to this article.
seen with manual injections of CO₂. Angiodroid now manufactures an automated CO₂ injector. Angiodroid is located in Italy, so it was perfect to interact with Dr. Palena for this.

We put together a single-center prospective study of 36 patients with critical limb ischemia and diabetes who all had chronic kidney disease classified as a stage 3 or worse -- advanced kidney disease. We were able to demonstrate that with the use of this automated injector you eliminate the problem of image degradation. Granted this is coupled with a special software for post-processing of the images, but we were able to obtain high-quality images even at the pedal circulation and it didn’t matter if there were occlusions or no occlusions. All these patients in the study underwent not only diagnostic CO₂ angiography but also underwent the intervention solely guided by CO₂ -- there was no further use of contrast media. There was contrast media used in the beginning to compare because you have to show the quality of images and compare. There were two blinded operators looking at the images, and the images were analyzed in terms of quality. There was no statistically significant difference in the quality of the images using one media or the other, despite the level of disease and despite the fact that we are talking about images even in the level of the foot. This finding is very exciting. A paper has been accepted for publication in the Journal of Endovascular Therapy.

**VDM:** So there were several things that were deterring physicians from using CO₂ previously that you think this could overcome.

**Diaz:** Image degradation was a big deal, and also when you have to use the manual device there were a lot of stopcocks and questions about the right way to do it without injecting air. The way that you connect this device to the side arm of the sheath is basically with one connection. There’s a filter, the catheter is purged once, and everything is controlled on a touch screen. It’s really simple, and it doesn’t take a rocket scientist to figure it out.

**VDM: So you’ve used the previous iterations and you find this was easier.**

**Diaz:** Yes. The first time I was going to do CO₂ imaging I thought, “How do I know that there’s no air in the line?” It’s kind of tricky to overcome that fear, and I think that gets in the way of many people actually doing this. But it is beneficial for us to be able to perform these procedures for patients because there is less risk of dialysis or worsening kidney function.

I can’t say there are no complications associated with the use of CO₂. It’s like everything else we do, but by following a series of prophylactic measures, you are going to obtain great images and you are also going to be able to help patients. It is important to keep in mind that we’re talking about infrainguinal disease. Some of the complications that have been reported with the use of CO₂ have happened with the treatment of iliac vessels or other abdominal vessels. When you’re using catheters in the abdomen and you’re using larger volumes of CO₂, complications can ensue. Operators need to become familiar not only with the CO₂ technology, but also with the volume. In our upcoming publication, Dr. Palena and I created a graphic illustration that shows per segment how many cubic centimeters of CO₂ were the typical volumes that we used. We talk about how we came up with the settings
and how much pressure should be administered. We go into detail answering all the typical questions that are going to come up: how do I set it up, how much do I have to inject, what pressure should I use, how is it not going to be painful to the patient, because I know that they have pain.

**VDM:** Any other tips or details about the learning curve when using the CO₂ device?

**Diaz:** For manual injections I think that after you’ve done 3 to 5 cases, it’s fairly self-explanatory. You get into the routine of purging the catheter and so on. The guide that Dr. Palena and I developed shows how to use the automated injector and how many cubic centimeters you will have to inject in each particular segment, because we go from the hip all the way down to the toes. Also we describe how to set up the pressures. We cover all those little things. I think if you are an experienced interventional therapist, one or two cases should be enough as long as you have in mind all of those particular little technical issues. Also, if your institution is going to actually make an investment to acquire this technology, there should be adequate support and you’re going to have people that are representatives that are going to come and do in-services and teach people how to use it and so forth, but it’s actually fairly self-explanatory.

**VDM:** But it’s not just for patients with kidney failure.

**Diaz:** Well that’s another adventure. Should we start replacing dye with this technology? You’re going to see people like me who are very excited about it and are going to say, “I don’t see why not,” and you’re going to see other people that say, “Why use CO₂ when you have risk of complications?” So, in the population that has chronic kidney disease level 3 or worse, it is justified. In people that have had allergic reactions to contrast media it’s justified. There’s no inherent nephrotoxicity, we produce CO₂ we have CO₂ in our body all the time. Right now those are the two populations where I think it is justified to use CO₂. As to whether we can extrapolate this to a more general application, stay tuned.