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Key Considerations on Catheter Based Renal Denervation in CKD

Dr. Caudle:

Welcome to *ASN Action Center* on ReachMD. I'm your host, Dr. Jennifer Caudle. And here today to discuss renal denervation as a treatment consideration for patients with CKD is Dr. Raymond Townsend. Dr. Townsend is a Professor of Medicine at the University of Pennsylvania and Director of the Hypertension Section at the University of Pennsylvania School of Medicine.

So Dr. Townsend, can you share what kinds of results have we seen with catheter-based renal denervation in clinical trials?

Dr. Townsend:

The answer to that question is a little bit bimodal, for lack of a better word. When renal denervation was first undertaken around 2007/2008, the results in drug-resistant hypertension were nothing short of spectacular. So, in a small study published by Henry Krum in *The Lancet*, the blood pressure reduction was huge. Office blood pressures dropped about 25 to 30 mmHg systolic within six months of having renal denervation done in people on five drugs whose office pressures were 180 or so, and that was an uncontrolled trial, and it was 50 people. Okay, it's a big splash in a very small puddle. Second wave of studies comes along, this time randomized to denervation versus no denervation, same idea: office systolic blood pressures quite high on many drugs, similar outcome in terms of blood pressure reduction, and that led to the clinical trial of HTN-3 done in the US, many centers, 2:1 randomization and with a sham control arm.

So, in the sham control arm, you did everything up to the point of randomization equally in the two groups, but on the table after the arteriogram is done and you're sure they're a candidate for denervation, two people got the procedure, one did not. But they had earplugs in listening to music, they had a sort of one of those masks you wear on a transatlantic flight to keep the light out of your eyes, so they were consciously sedated, so they didn't know whether they got denervation or not in a post-hoc test which they filled out said they didn't know. And the problem with HTN3 was, yes, the procedure worked, it lowered office blood pressure, this time in the range of 15 millimeters, but it lowered the blood pressure in the sham control group to a very close degree, only a few millimeters less. So that was the first peek in it.

What we have learned since then, and since time is limited on this podcast, I'll give you the skinny as far as I understand it where we are now circa 2022, the daytime and nighttime blood, the 24-hour blood pressure reduction that we see with renal denervation is somewhere on the range of 6 to 9 millimeters over 24 hours at a period of time between two- and six-months' post denervation. And the reason for that two to six months is as short as two, if you use ultrasound and no drug, you can see an effect at two months, and if you use radiofrequency energy, you need to wait three. At least that's been the protocol to wait three. And if you're on medication, whether you use ultrasound or you do radiofrequency energy, six months is the typical point.

The last thing to say about the kind of results we have seen with renal denervation is that in addition to essential hypertensives, the blood pressure also falls in those with CKD and those on dialysis and those with diabetes and those with isolated systolic hypertension. There's little nuances amongst those groups, but there's a large registry that Medtronic sponsored called the Global SIMPLICITY Registry, and there's also a growing registry that ReCor is sponsoring: that is the ReCor Paradise Registry. So there's up to three years' data on the radiofrequency, the Medtronic approach, and there will be many years' data on the ReCor approach as well, assuming things continue to go forward.

Last point about the catheter-based renal denervation is that even after six months, when you continue to follow these people, as Deepak Bhatt presented very recently at the TCT meeting, the blood pressure continues to fall up to three years, and so, at three years that, that 8 to 9 millimeters of daytime or 24-hour, and both of them look at blood pressure reduction, can be as high as 18 or 19 millimeters on a 24-hour systolic blood pressure at a point in which three years have passed, so it appears to work. It appears to work with or without drugs, and it appears to be durable.

Dr. Caudle:

Well, thank you so much for that excellent summary. You know, given these results, could a treatment option like this have long-term impacts for our patients?

Dr. Townsend:

So, as many people listening to this will be aware, many years ago, decades ago now, the FDA, when it was considering a drug for hypertension to be approved, ceased to require an outcome trial saying that, okay, if I treat someone with this ACE inhibitor versus nothing or versus a comparator, I have to take 10,000 people in each arm, follow them for five to seven years and show a mortality or some other important to the patient kind of outcome in order to get approval. The FDA has been in print with this, that if you reduce blood pressure, you by—you de facto improve cardiovascular risk, and that's allowed to be in the label. So, when you pull out these labels for any of these drugs that are indicated for hypertension, you will see that, that it reduces blood pressure and therefore reduces cardiovascular outcomes, and so it is anticipated that that will happen.

Now, we are monitoring these kinds of phenomena in things like the Global SIMPLICITY Registry, which has 3,000 people enrolled in it that have completed the three-year point, and we're putting another 2,000 in there because there's ongoing trials that we are recruiting, and once they finish in the clinical trial, they are automatically populating the SIMPLICITY Registry, so we'll have data on 5,000 people. And when you model what had happened to them had their blood pressure not dropped and they just were simply followed because they had no denervation and they stay on their three, four, five medications, whatever it is, and then you look at what happens to these people now that their blood has been reduced, well, on average, about 15 millimeters over the three years, the cardiovascular event rates: stroke, heart failure, death, etc., are diminished in the group that got denervation. And it's cause and effect, never can argue that, but at least it's a valid observation, that it appears that there is less cardiovascular risk in people because their blood pressure is lower when they have undergone renal denervation and have been followed out to three years.

Dr. Caudle:

Excellent. And I'd like to thank you, Dr. Raymond Townsend, for joining me to discuss renal denervation in patients with chronic kidney disease. It was great catching up with you today.

Dr. Townsend:

Thanks for the opportunity

Dr. Caudle:

For ReachMD, I'm your host, Dr. Jennifer Caudle. And to access this episode and others from our series, please visit ReachMD.com/ActionCenter where you can Be Part of the Knowledge. Thanks for listening.