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Complementary Treatment for Uncontrolled Hypertension: Using a Novel Blood Pressure Procedure

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Welcome to CME on ReachMD. This activity, titled “Complementary Treatment for Uncontrolled Hypertension: Using a Novel Blood Pressure Procedure” is provided by Medtelligence.

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[Chapter 1]

Dr. Townsend:
Despite the plethora of antihypertensive drugs and nondrug therapies available, hypertension remains undertreated and is the underlying cause of many cardiovascular comorbidities and mortality. However, with a procedure known as renal denervation, patients with hypertension may experience a significant, durable, and safe reduction in both systolic and diastolic blood pressures. Let’s review the renal denervation mechanism of action, the clinical trial data showing blood pressure reductions in patients, and how this may fit into your treatment algorithm.

This is CME on ReachMD, and I’m Dr. Ray Townsend.

Okay, let’s get started by reviewing the burden of hypertension and the limitations of currently available antihypertensive treatments.

So hypertension, a leading risk factor for cardiovascular disease – fairly easy to detect, and yet 30% of people are unaware that their blood pressures are elevated. Among the residual 70%, roughly half of them, 35%, are on therapy of some kind, but they’re just not controlled, and about 35% of people with hypertension are adequately controlled, given the current guideline-determined threshold for adequacy of blood pressure therapies. High blood pressure is just such a problem.

It is the leading global risk factor for death – premature death – and for living with a disability secondary to elevated blood pressure, like a heart attack or a stroke. In the world, whether you’re in a low-income, middle-income, or high-income country, it leads the list of the World Health Organization’s noncommunicable diseases as a contributor to premature death and living with what’s called a disability-adjusted life-year. Part of our concern with high blood pressure is the fact that we have more than 100 medications available. We have half a dozen different lifestyle measures that help blood pressure.

And yet, when you go into a hypertension clinic, where people are there specifically for blood pressure care, you will find that despite what a patient tells you they’re taking – I’m on 3 drugs, I’m on 4 drugs – about 44% of the time, a patient is taking at least 1 less medication than they declare when interviewed, and about 1 person in 6 – roughly 17% of patients with hypertension, particularly complex hypertension – are not taking any medications that can be detected in the blood or in the urine.

That covers the effects of uncontrolled hypertension and the role of the patient in adherence. Next, we’ll dive into renal denervation. Stay tuned.

[Chapter 2]

Dr. Townsend:

Welcome back. Now that we better understand the burden of hypertension and why medications and nondrug therapies are not the answer for many patients, let's examine the mechanism of action of renal denervation, or RDN.

So what happens with renal denervation has to do with the fact that there is cross talk between the brain and between the kidneys, and the nerves on the surface of the kidney arteries and the nerves in the brain stem of the central nervous system are in constant communication with one another, sending signals back and forth about the status of the circulation's blood pressure. In the last dozen or so years, it's been possible to interrupt that traffic between those 2 places – the brain and the kidneys – by virtue of doing something to the renal nerves we call ablation.

Ablation usually involves putting either temperature or a neurotoxin into the surface of the kidney artery, either by radiofrequency energy or ultrasound in the case of ablation, or absolute ethanol in the case of injection. And the idea is to cut the traffic between the kidneys and the brain, particularly in people with medications already on board whose blood pressure is not well controlled.

The catheters that are in use now are fairly small. The spiral catheter is well named because it assumes a shape that, once it's deployed in the kidney artery, it automatically curls, and the 4 electrodes from it touch the wall on the inside of the kidney artery and emit a cloud of radiofrequency energy, in the case of a radiofrequency energy catheter. And the energy heats up the fat around the kidney artery itself, and that fat contains the nerves that are ablated by the increased temperature. So whether you put temperature elevation or alcohol into that periadventitial space, you will reduce and in many cases eliminate the nerve traffic between the kidney and the brain stem in the interest of seeing blood pressure reduced.

Stay tuned, because our next topic will be the clinical trial evidence for blood pressure reduction with RDN.

[Chapter 3]

Dr. Townsend:
For those just tuning in, you're listening to CME on ReachMD. I'm Dr. Ray Townsend, and today I'm discussing how renal denervation reduces blood pressure in patients with hypertension.

Welcome back. We're turning to the clinical trial evidence for sustained blood pressure reductions in patients with hypertension. Let's look at the data.

In the last dozen years or so, especially after 2014 with HTN-3, the SPYRAL Clinical Hypertension program was initiated. After HTN-3, we went back to the drawing board and, very similar to the development of a drug for high blood pressure, the first question we addressed is: Does renal denervation really lower blood pressure in a hypertensive on no medication?

Okay, let's assume it does. So we started that particular thing, the OFF MED program, and then we said: Okay, let's assume that it's going to work; we've got a successful recruitment going. We want to know next how well renal denervation works in the presence of medications – 1, 2, or 3 meds. And then after that, we want to know what it does in the real world, not in the presence of a clinical trial. So that brought in the Global SYMPLICITY Registry, where people have been rounded up from many countries, because it's available in many countries, and are followed for 3 years after their denervation to see what happens to their blood pressure and to see how safe the procedure is.

So just to recap briefly, the OFF MED doesn't lower blood pressure at all in the presence of no medication for blood pressure. In the ON MED, does it lower blood pressure when there's someone else in the sandbox – 1, 2, or 3 meds? And then in the registry, how does it work in the real world, and how safe is it for things like kidney function and that kind of thing, and do we need to pile on medications at some future point in time?

For example, of the OFF MED pilot program, these were the first 80 people that were denervated in the absence of medication, and we found with ambulatory blood pressure monitoring, that we've got about a 5-mm, 24-hour systolic blood pressure reduction, and that was our signal to proceed with the next steps in the spiral program itself.

We also, of course, measure office blood pressure, and you will see in the renal denervation literature that typically in the denervation arm, the decline in office blood pressure is about 9-10, maybe 11 mmHg for office systolic. And that's very similar to most of the drug trials, where an antihypertensive medication being tested for registration, and ultimately approval, demonstrates a very similar degree of blood pressure reduction. Diastolic blood pressures fall as well, but the focus has largely been on the systolic blood pressure in the clinical trials to date. We use ambulatory because ambulatory gives us a fairly robust placebo effect, so if you don't do anything, you typically don't see any changes in the average ambulatory blood pressure profile in your control group.

With denervation, no matter how it's done, we see the 24-hour profile drop, night and day, and especially during the night, where there's a lot of data – research – to show that many of our hypertensive complications are more likely to emerge when the nocturnal blood

pressures are high – the so-called non-dipping status, where they don't fall compared to daytime or even the rise of status when they go up at night.

One of the things, mercifully, in this whole process has been the safety profile of all the denervation programs. We set a safety bar when we design these studies, in conjunction with the FDA, at about a 7% event rate around the time of denervation itself. So our concern was for hematomas, dissections, and those sorts of things, and we used things like the CORAL trial in the past, a renal angioplasty trial, to set the bar at 7%. And it turns out we have a very low incidence of events, whether they're clinical events like hospitalizations and urgent hypertension, versus periprocedural events, like hematomas and pseudoaneurysms.

And in the real world, in the SYMPLICITY Registry, we have about 3,000 patients enrolled, and 1 of the 2 lessons we've learned from the SYMPLICITY Registry is that blood pressure continues to fall after the first 6 months, which is a very frequent time used for an outcome determination. But we see, again, a 1-3 mm reduction in office systolic blood pressure or ambulatory 24-hour systolic blood pressure over time, out to 3 years. And we see that kind of occurrence in the absence of jacking up the medications.

So you get 3 years older, you expect your blood pressure to go up a little bit, but it doesn't. If anything, we see either a stabilization of medication and lower blood pressure or even in some people a small decrease.

How likely are we to get our patients to a guideline-directed degree of blood pressure control? The answer is it's about 3 times more likely that they'll get to a less than 130 or less than 140 kind of blood pressure compared to where they started.

And secondly, we have a fairly good safety record, even in the real world, because we've been tracking things like the kidney functions, et cetera, and so far we have not seen a signal that the natural changes in kidney function with age are accelerated in some fashion, and renal artery stenosis is not provoked by virtue of doing this.

That brings you to the issue of what do the patients think about this? So we did a study with 400 people called a discrete choice experiment, where we gave them a scenario. First, we made sure they understood blood pressure, its role in mediating organ damage, and the value in blood pressure reduction and the risks, both of medication – drug side effects – and denervation – periprocedural effects. And then we asked the patients, who were all uncontrolled – we verified that with the patient and their physician, and all this was done in an online survey – we said, "You're uncontrolled. Here's the data. What would you do? Would you want to take more medication, another medication, denervation, or just pass and just say, 'I'm satisfied with my current level of blood pressure'?"

And when we evaluated the responses in patients to these kind of questions, overwhelmingly the driver, for whatever answer they chose – more meds, denervation, whatever – was the magnitude of blood pressure reduction, so it was the elephant in the room. When patients looked at blood pressure benefits, they felt that those were more important than things like side effects, et cetera, in making a choice about what to do. And roughly, no matter where you do these kind of studies – and they've been done in Asia, Europe, and the US – about 30% of patients with uncontrolled blood pressures, higher than current guidelines suggest, they're willing to consider an intervention like renal denervation to enhance blood pressure control.

We also have found that providers are different than patients, in terms of their expectations. Providers tend to think that it's the magnitude of their blood pressure elevation at the time the decision is made and the number of blood pressure medicines they take that drive their decision-making process. But when we actually asked the patients, it's drug side effects that drive a lot of the patient decision-making in the process.

So there's room for this thing we call shared decision-making, to have one side talk with the other and ultimately come to agreement on the way forward.

Denervation's been taken up by both, for example, the US side in the SCAI [Society for Cardiovascular Angiography & Interventions] program and also the most recent European Society of Hypertension [ESH] guidelines. And it is now at the level of what we call a class IIB recommendation. The ESH guidelines moved it out of research only into potentially clinically useful, and they gave it a class IIB recommendation, and that is the same level of recommendation that spironolactone has in the ESH guideline.

Couple of things, then, just wrapping up here, and I have a handful of take-home messages. The first is that – and we've been asked this repeatedly – how long does this procedure last? We have clinical trial data that show that it lasts for at least 3 years. You don't have to repeat it. You don't have to do it every couple months or whatever – 3 years. It has a certain performance that is safe and without a lot of the things we associate with drug side effects – the swelling from calcium channel blockers, the cough from ACE inhibitors, and that sort of thing. And most importantly, I think, one of the most difficult aspects to managing, especially in the complex hypertensives, has been keeping them on their medications. And so with a procedure like renal denervation, adherence is not an issue because once the procedure is completed, we think that they are pretty good for at least 3 years, and in a couple of recent papers, we have data out to 9 years showing no loss of efficacy over the long haul.

That's all the time we have today. I hope this information about the potential benefits of renal denervation for blood pressure reduction in your patients with hypertension has been useful. Thank you for listening.

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