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## The Latest on Patients with Hypertension & CKD

### Dr. Caudle:

Treating hypertensive patients with chronic kidney disease, or CKD for short, can be challenging, and lifestyle modification and medications need to be carefully considered, but one treatment modality is gaining more attention than others. What do we need to know about it?

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. He's also a member of the hypertension group at the University of Pennsylvania.

Dr. Townsend, thank you so much for speaking with us today.

### Dr. Townsend:

Thanks, Jen. I'm glad to be on the podcast.

### Dr. Caudle:

So, to give us some framework for the discussion today, Dr. Townsend, can you tell us about the link between chronic kidney disease and hypertension?

### Dr. Townsend:

The first point to make is that high blood pressure is kind ubiquitous in an adult population, particularly one that has adequate if not excessive access to calories and to salt, which, unfortunately, characterizes our population in the US fairly well. We also know that blood pressure elevation is a function of age. So, as you age, your systolic blood pressure in particular kind of rises with each decade, and your diastolic does as well until you're in your 50s, and then it kind of plateaus, and if anything, it tends to fall after your 55th birthday. But the systolic rises relentlessly, especially with access, as I mentioned, to sodium. It's said that somewhere around 25 to 35 percent of the adult population in the US has high blood pressure, and it's also said that somewhere around 12 to 15 percent of the adult population in the US also has chronic kidney disease. Let's just use 30 percent incidence of hypertension in the adult population. Switch over to CKD and the prevalence of hypertension is more in the range of 80 percent and even a little higher as you approach the need for dialysis.

What makes hypertension such a unique link to chronic kidney disease is that all the things that are regulating your blood pressure—your sodium intake, the autoregulation that occurs at the level of the vessel itself, the circulating biomarkers like angiotensin II and norepinephrine, and things like that, and even the autonomic nervous system, which are carefully regulated in health, not only do they go awry in chronic kidney disease, as witnessed by the high prevalence of hypertension, but they also all go awry when it comes to hypertension and chronic kidney disease. So, sodium is a problem, autonomic is a problem, circulating factors are a problem, and even the crosstalk using nitric oxide at the level of the vessel is a problem in CKD. And the thing is that when you look at research which identifies one of those factors, all of them are present at the same time, which makes the treatment of hypertension and CKD such a challenge.

### Dr. Caudle:

And if we dive into this relationship further for patients with CKD and resistant hypertension, what sort of factors contribute to elevated blood pressure?

### Dr. Townsend:

So, Jen, I like to think of high blood pressure as a consequence or a result of the interaction of those four things I mentioned in answering your first question. And when it comes to sodium intake, well, you can recommend less salt, and people sometimes actually comply with that, but we have fairly good diuretics that get you at that consequence, and you can somewhat manage if not well manage the sodium aspect. For the biomarker aspect, we have drugs that interfere with norepinephrine or interfere with angiotensin II and it's possible to block many of the biomarker effects that circulate in the bloodstream. And even when it comes down to such things as the endothelium and the vascular smooth muscle interaction, calcium channel blockers, for example, help at the level of the vascular smooth muscle directly, so three of those four sides of that kind of quadrangle I like to use are fairly well addressed with our medication therapies.

Where we sort of fall a little short is our ability to really interrupt the sympathetic nervous system. Yes, we have alpha blockers, beta blockers and alpha-2 agonists, but in all candor, we're not really that good at truly impairing the sympathetic nervous system. It's been sort of a challenge because of the blood-brain barrier and other things that kind of limit the ingress of our meds, and so we're often peripherally managing the sympathetic but not getting to the brain as opposed to the heart of the matter itself, and that's where I think the new therapy, especially denervation of the kidney artery might be a step forward.

**Dr. Caudle:**

Well, thank you for that. And let's talk a little bit more about the treatment options. You know, how does catheter-based renal denervation work to lower blood pressure?

**Dr. Townsend:**

If I knew the answer to that, I would be a lot more confident in the intellectual content of this podcast because to be truthful, we suspect that one of the main ways in which renal denervation works is to interrupt the crosstalk between the kidney and the brain. We used to say that the kidney was a consequential organ when it came to central, autonomic, sympathetic that is output. So the kidney receives sympathetic signals, and the work of Gerry DiBona and Ulla Kopp and others looking at the relationship of sympathetic function and the kidney will tell you that when you zap the kidney's sympathetic nerves, the first thing you get is a bit of renin release. The next thing you get is more sodium reabsorption, and then finally, you get vasoconstriction as you jack up the intensity of the sympathetic stimulus.

What we have learned is that there's also signals going from the kidney to the brain. So, when renal denervation is undertaken, one of the things we think happens is that you interrupt the bidirectional traffic on the surface of the kidney artery that links the parenchyma of the kidney to the vasomotor centers in the brain and brain stem that control blood pressure, so sympathetic interruption we think is a major mechanism of action of renal denervation. What does it do to the non-sympathetic nerves? Well, it blasts them too. What's the consequence of that? Truly, we really don't know. The thing is, and one of the crazy things about the kidney is that there's remarkably little evidence that there's parasympathetic innervation in the kidney, so the natural balance to the sympathetic in many organs is the parasympathetic, but as far as I know, there's very little evidence that we have much in the way of parasympathetic innervation of the kidney. So I think sympathetic is the major key to understanding renal denervation's effects, at least in terms of what they do to the autonomic nervous system.

**Dr. Caudle:**

Thank you very much for that. For those of you who are just tuning in, you're listening to *ASN Action Center* on ReachMD. I'm your host, Dr. Jennifer Caudle, and today I'm speaking with Dr. Raymond Townsend about renal denervation as a treatment consideration for patients with chronic kidney disease.

**Dr. Caudle:**

Renal denervation is included in the European Society of Cardiology and European Society of Hypertension guidelines. Before we close, Dr. Townsend, do you think the US is heading in this direction?

**Dr. Townsend:**

I wish. I'm glad you're not from Wall Street asking me that question, or I'm glad you're not a payor asking me that question. I'll tell you how I understand things to go here, and after that it's really up to the deities that control these kinds of phenomena to answer that question. It's not approved in the US, so nothing is going to happen in terms of a guideline until an approval occurs. And even with an FDA device approval here and actually making it available, someone's got to pay for it. Whether CMS will allow for this and pay for it, that's another hurdle to get through. And if CMS and others pay for it, then there's the issue of will physicians recommend it or will the patients accept it. So there are a couple of those Whac-A-Moles that kind of crop up here when you're trying to do forecasting on what will happen to this. And if it's approved, if CMS agrees to pay for it, if other independent insurers agree to pay for it, if physicians will recommend it and if patients are willing to undergo it, and they're willing to trade those risks for very small amounts of blood pressure—assuming all that happens, then it becomes an issue of the guideline people saying, okay, do we have enough evidence: A) that this works, B) that this works with meds, and C) that this works in a variety of populations. Does it work in the melting pot, if you will, of

people we have here in the US? Is it safe in addition to being effective? And is it likely that the costs of this procedure, which are not inconsequential, will come down over time? And will we be able—final point here—will we be able in the future to figure out who is the best candidate for this?

Because like any drug we use for hypertension, no drug has 100 percent response rate. Most antihypertensives for blood pressure will lower your systolic 10 millimeters in about 60 to 75 percent of the people, which means that roughly 1/4 to 1/3 don't respond, and that's what we see with RDN. There is a population that doesn't respond. Figuring out who they are would be a great leap forward for the field, but in the meantime, I'm hoping that US hypertension guideline writers will at least give a consideration even if they choose to say it should only be done under X, Y, or Z circumstances.

**Dr. Caudle:**

Excellent. And with those interesting thoughts in mind, I'd like to thank you, Dr. Raymond Townsend, for joining me to discuss renal denervation in patients with chronic kidney disease. Dr. Townsend, it was wonderful speaking with you today.

**Dr. Townsend:**

Jen, it was a pleasure, and thanks for the opportunity.

**Dr. Caudle:**

Excellent. And for ReachMD, I'm your host, Dr. Jennifer Caudle. And to access this episode and others from our series, please visit [ReachMD.com/ASNAActionCenter](https://ReachMD.com/ASNAActionCenter) where you can be Part of the Knowledge. Thanks for listening.