DR. ROB SIMARI: Greetings, I'm Rob Simari of the division of cardiovascular diseases at the Mayo Clinic, and today I'm pleased to be joined by Dr. Rajiv Gulati, one of the leading interventionalists at the Mayo Clinic, to talk about a topic that has been very exciting over the last few years and that is the topic of renal vascular denervation. Rajiv, it seems to me like the thought of an interventionalist treating hypertension with a catheter must be the old analogy of to a man with a hammer, everything looks like a nail. So this is a great opportunity to talk about a field that has been very exciting. Tell us how the field of renal vascular denervation was developed.

DR. RAJIV GULATI: Yeah, thanks Rob. This is a great chance for us in the cath lab to rebrand ourselves as preventative cardeologists, I think, to treat hypertension. But this is a really fascinating story-- I won't go into too much detail because I think we've known for a number of years the importance of the sympathetic nervous system in hypertension. What is now becoming increasingly clear is how important the kidney is as a sensor of hypertension to modulate sympathetic nervous activity. So the data and the thinking comes from surgical sympathectomy back in the '40s and '50s, which was the only treatment for hypertension. Worked incredibly well, but was beset by problems with orthostatic hypotension, autonomic problems because of complete sympathetic nervous transection. And now there's this ability to kind of nicely modulate sympathetic activity by focusing an ablation on the renal nerves to effect both sympathetic efferent outflow at the kidney level, and also effect afferent nervous system discharge to the brain, thereby reducing chronic sympathetic over activation.

DR. ROB SIMARI: So was it technology that drove the opportunity, or was it unmet need that drove the technology?

DR. RAJIV GULATI: I think it was more likely the former. This recognition of the importance of the sympathetic nervous system-- of sympathectomy being a really brutal way of treating hypertension. And then with the development of these ablation catheters that can focus ablation. So it seems more that the technology has enabled this to be potentially a widespread technology.

DR. ROB SIMARI: So there's been a number of ongoing large scale international clinical trials. Catch us up on where the evidence for renal denervation is in the treatment of hypertension.

DR. RAJIV GULATI: The evidence began with a single case report, then a case series, then a randomized study in the simplicity two study done mostly in Europe and Australia of patients who underwent denervation who were compared to historic controls who didn't undergo the procedure. And it showed a clear reduction-- sustained reduction-- in blood pressure in those treated with denervation. Around about 30 millimeter systolic and 12 diastolic, that's now sustained out to two years. The criticism of that study was this was not a sham controlled procedure. So of course there's the potential for effects due to lifestyle changes in those who were treated. The simplicity 3 study-- which has just finished recruiting in the US-- addressed that. It was a much larger study-- 530 or so patients randomized two to one to denervation versus sham.

DR. ROB SIMARI: And these are patients with resistant hypertension as evidenced by--

DR. ROB SIMARI: Resistant hypertension with a systolic of 160 or more, diastolic of 90 or more on optimal doses or maximally tolerated dose of three drugs, including a diuretic. Good going hypertension and good medical therapy.

DR. ROB SIMARI: And so when will the results of that trial be available?

DR. RAJIV GULATI: Well, we finished recruiting now, so we're hoping to hear within six months maybe some of the early data. Medtronic-- who sponsored the trial-- will have that information. But six to nine months is the projected time frame.

DR. ROB SIMARI: And the primary endpoint was blood pressure control.

DR. RAJIV GULATI: Six months offers blood pressure reduction.

DR. ROB SIMARI: So we have learned from coronary vessels, as well as pulmonary veins, that putting energy across the vascular bed has a potential downside. What's the potential downsides of renal denervation?

DR. RAJIV GULATI: Yeah, I think that was when I first heard about this technology-- I was initially quite skeptical because putting a catheter into a vessel and deliberately damaging from the intima out the adventitia didn't seem logical to me. But I think we've been surprised at the lack of acute technical complications. There have been reports of an occasional dissection of the renal artery, which is a natural consequence of guide incubation and inserting a catheter, but that's been remarkably few. The concerns that some people are expressing that many of us have are the risk of a restenotic phenomenon down the line, so response to injury-- 6, 9, 12 or longer time period after the denervation. In the early studies, that doesn't seem to be a major signal for significant restenosis. But I think time will tell.

DR. ROB SIMARI: So the enthusiasm for this technology is not limited to hypertension. Tell us, what other directions is the field going in?

DR. RAJIV GULATI: Yeah I think that's probably, if anything, the most exciting aspects of renal denervation. So this concept of chronic sympathetic nerve discharge from the brain being a principle pathophysiologic contributant to a number of disease processes lends the possibility that denervation can treat multiple diseases. And there are small studies and sub studies that suggest that renal denervation will reduce recurrence of AFib after pulmonary vein isolation will improve glucose tolerance, will reduce sleep apnea, and may even modulate heart failure. These are just some of the things that have been looked at. And I think we should stress that these have been small studies, not well-controlled, but certainly have raised eyebrows across the spectrum of preventative cardiology as maybe a paradigm shifting technology.

DR. ROB SIMARI: So if you had to-- if you got at your crystal ball and tried to predict where we would be 10 to 15 years from now, what would you predict the role of denervation might be in clinical medicine?

DR. RAJIV GULATI: Yeah I guess there's a spectrum of possibilities. This could fail if the simplicity three study shows no effect or raises a signal for major harm, we could be stopping this in the very near term. That seems unlikely. More likely this will find a role that may be not as extensive as we're all hoping for, but significant nonetheless. I think recognizing that most people don't want to take hypertensive medications. Those that do are quite often beset by side effects. So there may well be a role for this in patients who don't want to or who can't take medication, those with metabolic syndrome, and hypertension pertains to a highest risk of cardiovascular endpoints. They'd benefit the most from denervation which seems to address a number of the problems in that disease process. I think the technology will improve considerably, I have no doubt about it. Right now it's a transfemoral six or eight French device. I'm sure that people are looking at getting a trans radial device that you can imagine, you can envisage a small Cath lab or fluoroscopy suite where people come in, have a procedure within 15-20 minutes, transrate it in, and then go home the same day. So there's a potential for this to be a relatively low risk, high frequency procedure.

DR. ROB SIMARI: And given the breadth and depth of the market, there's been a lot of competing technologies that have been developed. Are there opportunities for further development, or do you see that they're going to have the same challenges as the current devices?

DR. RAJIV GULATI: Yeah, I don't know is the short answer. There are I think at the last count 55 registered companies with some technology in this field, so there's considerable impetus and excitement behind it. Some of the challenges will remain. This is still an invasive procedure. There's still a concern about reinervation three, five years down the line. I have to say the early studies haven't raised that as a serious concern. But these things are going to be challenges that will need to be addressed.

DR. ROB SIMARI: Thanks Rajiv for a very interesting discussion, a very exciting field that may in fact someday change the way we practice medicine. And thanks to our viewers for being with us today on this video podcast for theheart.org from the division of cardiovascular diseases. We look forward to seeing you in the future.