

Melanie Cole, MS (Host): Welcome to the podcast series from the specialists at Penn Medicine. I'm Melanie Cole. And today we're talking with Dr. Benjamin D'Souza. He's a cardiac electrophysiologist, associate professor of clinical medicine at Penn Cardiology and the principal investigator for the assessment of implantable cardiac contractility modulation in the heart failure group with higher ejection fraction or the AIM HIGHER study at Penn Medicine.

Before we begin our discussion today, I'd like to remind our listeners that information about participation in the AIM HIGHER study at Penn is available by calling 215-662-8562.

Dr. D'Souza, thank you so much for joining us today. We're talking about two things here today: heart failure with preserved ejection fraction or HFPEF, which has been called an epidemic in the United States, and the AIM HIGHER study, which concerns a related therapy.

As we know, HFPEF is defined as cardiac ejection fraction of greater than 50% or normal ejection fraction coupled with the symptoms of heart failure. How is it possible, Dr. D'Souza, for the heart to be both failing and capable of normal ejection fraction?

Dr Benjamin D'Souza: Thank you, Melanie. That's a good question. I'm happy to answer that. If you think about the heart, you can think about the heart squeezing, and you think about it relaxing. And so when a heart doesn't squeeze properly, that's what we refer to as heart failure with a reduced ejection fraction, commonly known as HFrEF. And then if you think about a heart that cannot relax properly, that is what's referred to as heart failure with a preserved ejection fraction, meaning that the heart is not relaxing properly. And if you think about it, if blood can't go forwards, it goes backwards and gives a patient the symptoms of heart failure.

Melanie Cole, MS: It's an interesting study. It's an interesting topic today. And you and I were discussing a little bit off the air about our field. So as we're thinking about this and talking to other providers, I'd like you to define the HFpEF population for us, and how is heart failure with preserved ejection fraction different from that of reduced ejection fraction. Speak a little bit, expand on that for us.

Dr Benjamin D'Souza: Sure. It's a good question. Unfortunately, the majority of the therapeutic options that we have in patients who have heart failure, which is millions of Americans, is largely based on patients with a weak heart muscle, again, HFrEF, that would be medications or procedures that we, you know,

performed as electrophysiologists. Unfortunately, the majority of those therapeutic options have not been successful in this patient population. And this is not a small number of people. If you actually look at the population, it's kind of split 50/50 between HFpEF and HFrEF.

So, you have millions of Americans and you have a therapy option, that everything else has not been shown to be helpful for the most part. That's why this study is particularly exciting because it'll open up an opportunity for us to treat these patients better than we have in the past. And that is why we're super excited about running this clinical trial at Penn.

Melanie Cole, MS: So as you just answered part of my next question in your last answer here, and the continuing need for effective therapies in patients with HFpEF has been called one of the greatest unmet needs in medicine today, I'd like you to speak about why it's simpler to arrive at treatments for other forms of heart failure than it is for HFpEF. We've been dealing with heart failure for a long time.

Dr Benjamin D'Souza: It's a good question. Unfortunately, as our population continues to grow and age, we just continue to have more and more people that are admitted to the hospital, and it's sort of stripping the resources of us to be able to care for them. Keeping people out of the hospital has clearly been shown to be an important metric. So, any concept that would potentially be able to help these patients we're all very excited about because as I had mentioned, unfortunately, many of our previous clinical trials for other either devices or medications have failed this patient population. As the numbers continue to grow and we don't have options to be able to treat them, that's where cardiac contractility modulation, also referred to as CCM, is a potential exciting opportunity to help not just make these patients feel better, but to keep them out of the hospital, which again, is one of the most important metrics that we've been looking at in our field.

Melanie Cole, MS: Well then, let's talk about that, Dr. D'Souza. The treatment you're investigating in AIM HIGHER is that device that you just mentioned known as the cardiac contractility modulator or CCM. Tell us a little bit about the AIM HIGHER study and its objectives. How did you become involved and what exactly are cardiac contractility modulation devices?

Dr Benjamin D'Souza: So, lots of interesting points. At Penn, we like to be the first folks in the country, let alone the world, to be able to offer groundbreaking therapy. And this certainly fits that bill. We've been involved in many clinical trials for this device that, again, I'll refer to as CCM. So, what CCM is, is again

cardiac contractility. And what the device actually does is it delivers electrical signals to the heart and, actually, a very large amount of energy. It's actually more than a hundred times the normal amount of energy that a pacemaker delivers. And the device is very similar in look and procedure to a pacemaker, but it is not actually a pacemaker.

We were involved in some of the very initial clinical trials that got this device approved for patients with HFrEF, with a reduced ejection fraction. And as part of those clinical trials, we found that there was a subset of patients that benefited from this, and that benefit is not just feeling better, being able to do more activity, improved quality of life, but also keep you out of the hospital, which again is very important as we mentioned earlier. There was suggestion that those patients with HFpEF may also benefit. So that is the goal of the AIM HIGHHer clinical trial, essentially a trial in patients in which we implant this device and follow them to see if they gain benefit, not just symptomatically, but also keeping them out of the hospital.

Melanie Cole, MS: Tell us a little bit about the procedure and what that involves. You're speaking to other providers. Give us some of the technical considerations that you were looking at as you were performing this and you were the first, as I understand, in Pennsylvania to implant the AIM HIGHHer study CCM device for HFpEF. So, tell us a little bit about what you were hoping for as far as outcomes and anything technical you'd like to let other providers that are really interested in this know about.

Dr Benjamin D'Souza: Of course. So, anytime you think about a new therapy, a new device, a new anything, you have to think about benefits and risks to the patient. Well, it turns out while this device is pretty fascinating, it is not an overly complicated procedure, as opposed to some of the other things we do in electrophysiology. The device, as I had mentioned, has two pacemaker leads that are implanted into the heart, either on the right side or the left side of the body. Those pacemaker leads hook up to a generator, and that generator essentially allows that energy to be delivered. Now, the patients, if done properly, do not feel the therapy. And the way that this device actually works is as we deliver that electrical energy over time, it actually reverses some of the genes associated with heart failure. And that's how the device works.

And another really fascinating concept about this device is the battery is self-charging. So, the patients get a wand and they put the wand up to basically their chest, just like you would charge your phone and it essentially can charge the battery indefinitely. So, the battery never needs to be changed for this device. So, that is also a novel part of this technology and something that is very

exciting to us. But from a technical standpoint, this procedure only takes about 30 minutes. It's a same-day procedure. Patients come in the morning, and they go home that day. Generally, it's a safe procedure. The risks are quite low. And as you had mentioned earlier, we were lucky enough to be the first ones in the state of Pennsylvania to implant it. And we're excited to do many more, and hopefully show that this therapy benefits this, again, continuing to grow millions of Americans across the country.

Melanie Cole, MS: It's very exciting technology and real advancements in heart failure, which as we've said is really an epidemic. And as our population grows older and lives longer, we're seeing more of this and just such an interesting topic. Finally, Dr. D'Souza, what sets the HFpEF program at Penn Medicine apart? What would you like referring physicians to know if they have a patient with suspected HFpEF? And when would you like them to refer to the specialists at Penn medicine?

Dr Benjamin D'Souza: Yes, that's a good question. As I mentioned earlier, what we pride ourselves on at Penn is that we are able to offer therapy that potentially patients can't get at other local or regional hospitals. We again like to be the first of folks and we like to provide therapy. And for any of you who've cared for these patients, it's very difficult because, as I had mentioned earlier, every known therapy that has been shown to benefit patients with heart failure and reduced ejection fraction does not benefit these patients, and our providers struggle with getting our patients in. So, what I would say is like any therapy, the sooner, the better and, you know, referring patients. And if you're not sure, please reach out to us, and we can walk our patients through the potential options for whether it be participating in the AIM HIGHHer clinical trial with CCM or other medications or device therapies that, again, we will continue to be at the forefront of medical technology.

Melanie Cole, MS: Thank you so much, Dr. D'Souza, for joining us today and telling us about the AIM HIGHHer study at Penn Medicine. To refer your patient to Dr. D'Souza at Penn Medicine, please call 215-662-8562, or our 24/7 provider-only line at 877-937-PENN, or you can submit your referral via our secure online referral form by visiting our website at penncardiology.org/referyourpatient. That concludes this episode from the specialists at Penn Medicine. I'm Melanie Cole.