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Are VADs the Answer to the Heart Failure Epidemic?

Narrator:

Welcome to Medical Breakthroughs from Penn Medicine, Advancing Medicine Through Precision Diagnostics and Novel Therapy.

Dr. Caudle:

In the United States, there are far fewer hearts available for transplantation than patients living with end-stage heart failure who need them. To offer hope for these gravely ill patients, new developments and practice innovations with cardiac assist devices are critically important.

You're listening to ReachMD, and I'm Dr. Jennifer Caudle, your host. With me today is Dr. Eduardo Rame, Medical Director of the Ventricular Assist Device Program and Associate Professor of Medicine at the Hospital of the University of Pennsylvania. We'll be talking about updated clinical approaches to heart failure and roles of ventricular assist devices, or VADs.

Dr. Rame, welcome to the program.

Dr. Rame:

Thank you, Dr. Caudle. It's a pleasure to be here with you guys.

Dr. Caudle:

Well, we're definitely happy that you're here. So, let's jump right in. To start, can you talk to us a little bit about heart failure in general? Can you maybe talk a little about the prevalence and the different stages of heart disease and how it's currently defined?

Dr. Rame:

We have an unmet need in heart failure in the United States and really worldwide. The unmet need is driven by, really, two important realizations. One, we still have not figured out the affliction, the actual disease progression of how somebody begins with an insult, whether it's a myocardial infarction or a viral infection or any other insult which the heart takes, and then how the heart in its adaptations does okay at the beginning, but then somehow, despite some of the advances in device therapy, there's still a disease progression. So there is a progression inherent to the deflection that does not allow us to say that this person has had a complete reprieve from having symptoms in the future.

Secondly, because we are the victims of our own success in cardiovascular medicine, people that are living longer with myocardial infarction, living longer with severe episodes of cardiogenic shock that are able to be supported with mechanical assist devices, temporary as well as with management strategies that have been deployed with intensive care units. These patients survive, but they survive with heart failure, so that is where we go to the numbers and see that there is a still growing epidemic with a high incidence in heart failure. You have 5 million patients in the United States with estimates as recent—within the last 10 years that will be increasing upwards of 7 million within the next 5 years having a diagnosis of congestive heart failure. And of those, you can kind of as a rule say the rule of the last 10 years, it's been the rule of 5, so 5,500,000. That's been sort of what's been discussed in terms of 500,000 having advanced heart failure, meaning that they've had a shot to improve with medical therapies and standard device therapies such as cardiac resynchronization and they have not. So, what's left in these patients, if it's really 500,000—and I say that because it's a large number of patients—is to be able to palliate them despite having a very low ejection fraction, or consider heart transplantation, or consider left ventricular assist device either as a bridge to heart transplantation or as destination therapy.

Dr. Caudle:

Before we go to our break, I think I definitely want to talk a little bit more about these ventricular assist devices and when the best time is

for a patient with heart failure to be referred to a heart failure cardiologist or a ventricular assist device specialist. Can you just mention that a little bit? Based on what you've already described, when is that best time for that patient?

Dr. Rame:

Let me just start by noting that there has been a lot of academic work in trying to define this risk in terms of risk models, so-called risk scores. And just to be fair in the field, each of these risk scores originates from a certain population that's local, sometimes multicenter, but just to be fair, even if multicenter, it can't be extrapolated to the rest of the world, certainly not across the Atlantic and so forth, so it is important to be, as a field, consistent with who are the patients that really need attention from an advanced heart failure group that's going to say to them, "This is your time to need surgery for heart failure, which includes a left ventricular assist device or a consideration for heart transplantation." And I believe strongly like that time should be based on the primary clinician that knows them—the primary care physician, the primary cardiologist, the experienced team of electrophysiologists or interventionalists who know the patient—when they say, "Look, we've done what we can; we've deployed device therapy to help the heart get better; we've deployed stents to help revascularize the patient even though he'd already been revascularized 20 years ago; and despite all that and good medical therapy, the patient's failing." I think the earlier the better, Dr. Caudle, is one of the important principles. And the second principle is, you're so used to seeing your patient over years, and on any given day they may look well, but it's important to listen to the patient. They often have a trajectory in their mind that's really spot-on, when they know that although they've got good days and bad days, the good days are no longer that great. There's been a decline. And if you could take a photograph of a patient when you first meet them—let's say you know them over 10 years—and then look at them again, the time you see them 10 years later, you'd say, "Oh, my God, there's been a cachexia that's developed, they look more ill," for whatever reason. There's a frailty that may set in. All of that needs to be taken into account in terms of timing, because what happens is people underestimate how much an acute decompensation, an acute heart failure hospitalization, can really turn a patient into a very sick-looking individual, and the fear is that the experts who do advanced heart failure will say, "Oh, my God, it may be too late."

Now, it's important to note that a lot of us in the field do realize that there is a component of frailty and acute illness. In other words, it could be reversible with better blood flow, with better support or just with some time after an acute decompensation, and that is why—along with what I said in terms of having the patient be very keenly phenotyped as far as are they worse off, is their functional capacity worse—you get data points like a cardiopulmonary stress test where the oxygen consumption is dropping from 2 years to now, or last year to now. That's a signal that something's going on; something's changing in the adaptation to a weak heart. Secondly, kidney dysfunction could be a signal. Out of the blue and especially if unexplained in someone who's got a cardiomyopathy, it's likely heart-failure related. Thirdly, you also have patients that lose weight unexpectedly, and that cardiac cachexia is a definitive signal for us that we need to consider intervention, or at least be happy with family meetings that we're going to be treating, especially an elderly patient, more palliatively and compassionately and not push the envelope too much with advanced therapies that are a challenge for an individual.

Dr. Caudle:

And that's excellent advice, actually. I'm kind of listening, and you mentioned so many really great points that apply to medicine in general. This idea of "the earlier the better" you mentioned in the beginning of your answer in terms of referral, and also being mindful about how we see our patients. I do think that sometimes it's difficult as time goes on and on to really think about how they are now versus how they might have been 10 years ago, and sometimes it's hard to see.

Dr. Rame:

Yes.

Dr. Caudle:

I think those are a lot of great salient points for any clinician just about how we manage our patients, and the idea also of consulting our colleagues and say, "Hey, let me just run this case by you. Let me just get a second opinion or some thoughts." So that's excellent.

If you're just joining us, you're listening to ReachMD, and I'm your host, Dr. Jennifer Caudle. I am speaking today with Dr. Eduardo Rame about the New Insights on Heart Failure and Updated Roles for Ventricular Assist Devices.

Talking about ventricular assist devices, putting these in the spotlight, how do patients with advanced heart failure generally respond to the placement of ventricular assist devices, and are there certain factors that are predictive of better outcomes for these patients?

Dr. Rame:

Yes, Dr. Caudle, this is a great way to initiate our discussion on assist devices is to really put the question, first of all, what is the expected response to mechanical unloading of the left ventricular with an assist device? and secondly, how do they do given that response in terms of how ill they are at the time going into this operation?

The way I would approach answering this, first let's take the latter half, which is: How do patients do with a ventricular assist device? This is an operation. In some centers it's an open-heart surgery with a sternotomy. In other centers they may do a more minimally invasive approach with a lateral thoracotomy. Many variations of that are now being generated with some hope in the field that it's going to lessen the surgical impact and improve our patients' recovery while not compromising on any of the success we've had with implanting these pumps.

The current era with the most recent results, and these come from the HeartMate III that was randomized to the previous generation HeartMate II as well as the other continuous flow device, the HeartWare HVAD, HeartWare Medtronic now HVAD, which got randomized in ENDURANCE to the HeartMate II. And the good news is we saw in these pumps, in these most recent trials, improvement both in the survival and in the adverse events but still are working to decrease the adverse events even more, decrease the rate of stroke, if possible understand why people have gastrointestinal bleeding and decrease that, and finally maintain or decrease the rate of infection as well. So that is the answer to the second question of how people currently in the current era now with over 20–, 30,000 pumps of each type implanted across the world are doing with the expectations we have.

To answer your first question of how well does the left ventricular assist device reverse the heart failure syndrome when we turn that pump on, the good news is we're also gaining more insight into making sure that with testing and good clinical follow-up, we really have that continuous flow pump set at the right speed and the right degree of support so that patients who underwent this incredible, challenging surgery can have full maximum benefit, and we're still learning how to do that in the field with intermittent hemodynamic monitoring. Maybe now that there's going to be sensors that are being developed like the CardioMEMS sensor that measures pulmonary pressure continuously over time, or at least can do so and you can get snapshots of it that are numerous, you can actually say, "Wow, I'm going to unload the heart more and make the patient even better and decongest them more." But, Dr. Caudle, just to answer your question, I do believe the pumps have the potential to reverse heart failure if the management is applied correctly.

Dr. Caudle:

My next question is about the types of mechanical circulatory support that they provide. What are these various types of mechanical circulatory support with respect to both short-term and long-term interventions?

Dr. Rame:

Well, it brings into light the possibility of having short-term, temporary circulatory support, which is, in the case of cardiogenic shock, essential if the patients appear to be climbing on their inotropic support requirement. We know from several registries and from the shock data that's been shared by industry and also by single-center studies that the degree of support from the point of view of how many inotropes a patient requires in cardiogenic shock correlates with the outcome. A poor outcome with low survival rates is expected when somebody is requiring more than 3 inotropes or pressors, and that makes sense. They're so sick they need this much support. But the other flip side is, of course, "Well, can anything be done? Is it too late?" That's where you've got to get in the clinical arena and in the studies that are going to be done the idea that if you could deploy a mechanical support platform like a temporary left ventricular assist device—and the examples here are Abiomed Impella support or TandemHeart support for the left side—if these patients could undergo that kind of support early on and if the complication rates from these pumps—and that's important to stress—are low enough, people could survive more if that were done. The bad news is some of the clinical trials that have compared these percutaneous left ventricular assist devices to an intraaortic balloon pump... which should not be at all given a light that it's not effective because a balloon pump, despite other studies which were done mostly in myocardial infarction shock, can effectively in certain individuals improve perfusion and circulatory support enough that the patient can get out of a pickle in cardiogenic shock. But unfortunately, the studies which were comparing balloon pump to the percutaneous LVADs have not shown a survival advantage of the percutaneous LVADs, but I have to say this is where we haven't done enough to make sure and classify patients well within the shock category so that we're really comparing apples to apples.

And the second thing that's important here is it's also important to realize that when you're in deep shock with a lot of tissue and organ injury and struggling to maintain a blood pressure on a lot of pressors and intubated and etc., etc., these patients may be too ill to have circulatory support be able to give them 100% likelihood to survive. It's still important to consider it, and I've seen patients survive even deep shock with temporary support, but boy, wouldn't it be better if we could have the staging of shock applied in a way that you say, "My gosh, this patient is truly refractory, I've got to intervene now before they get so sick," and have those outcomes be demonstrated of improvement in those patient populations that are not yet in the deepest stages of shock?

Dr. Caudle:

Are there any particular limitations to ventricular assist devices that are currently being investigated or improved upon by your peers?

Dr. Rame:

Yes. So, number 1, the durability of the left ventricular assist device to support the patient with chronic heart failure depends on not just

the, if you will, biocompatibility of the pump interfaced with the patient, and that has to do with the ability of the blood to not be too traumatized by a pump. After all, we have blood flowing in the channels of a pump that's generating flow within the human body to support the patient, so there's that concept of biocompatibility which then leads to: Does this pump create thrombus? Does this pump create also a scenario where it could lead to gastrointestinal bleeding?—which is what we're seeing to some degree, is that some of the gastrointestinal bleeding has to do not just with how sick the patients are from heart failure perspective and the inflammatory response to that, especially when they have surgery with a pump, but also the blood trauma that then doesn't allow all the blood components that are usually there to keep in check our bleeding tendencies. I mean, we're human beings with lots of checks and balances to make sure we don't bleed versus clot and so forth. That whole paradigm is very much challenged on the pump. Thank God it's not a major problem where it's above 50%, this problem, but it's important and humbling to know that when you put a left ventricular assist device, you need to consent the patient that they need to expect up to 30% likelihood that they could have gastrointestinal bleeding. And a percentage of those patients, maybe 5 or 10%, could have recurrent GI bleeding, meaning then you're going to have the problem come up again and again and again because we don't understand the affliction specifically. So that's an important limitation of the technology, is how to improve the biocompatibility and decrease the adverse events.

A second important limitation that I've already alluded to probably twice in this interview is the health of the right ventricle over time. You're supporting the human body when it's really sick with heart failure with a left ventricular assist device, not with a left and right ventricular assist device. The right ventricular assist devices are deployed sometimes when the patient absolutely is going into the surgery with no reserve, no capacity for the right ventricle to do well perioperatively, and it's being deployed, the right ventricular assist device, either temporarily with some platforms that are both being developed percutaneously and surgically, and those platforms are present and are being used by centers—others are, like I said, being developed so that we have better, better pumps for the right side—but that's a really important limitation to share with your patient and your colleagues that even if you get an LVAD with a terrific right ventricle at the time, the disease state of heart failure, like we talked about, is progressive, and some patients will develop what we call late right heart failure where the right heart is, for whatever reason, not completely understood, not able to rise to the challenge of maintaining good function and being able to allow the patient to do things as well as they did, let's say, if they had their pump implant 2 years ago and they're developing now more signs of edema, more signs of a diuretic requirement, more signs of fatigue. Those patients may actually have a right heart that needs some improvement, and that's what a lot of us are working on now.

Dr. Caudle:

This was a really amazing discussion, Dr. Rame. I really appreciate all of your time and your attention to a lot of ins and outs of ventricular assist devices and heart failure for myself and for our listeners. I'd like to thank you, Dr. Eduardo Rame, from the Hospital of the University of Pennsylvania for joining me. Dr. Rame, thank you for being here.

Dr. Rame:

Thank you.

Narrator:

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