Podcast Series: Heart Failure Podcast Series
Episode Title: **Device Therapies for HFmrEF/HFpEF**

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00:00:05.600 --> 00:00:16.629
Andrew J. Sauer: Hello, and welcome to the American Heart Association's Heart Failure Podcast Series. This episode is titled, Device Therapies for Mildly Reduced and Preserved Ejection Fraction Heart Failure.

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00:00:17.010 --> 00:00:26.530
Andrew J. Sauer: This program has been created and directed by a volunteer planning committee. Funding for this American Heart Association educational program has been provided by Bayer.

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00:00:26.590 --> 00:00:39.519
Andrew J. Sauer: I'm Andrew Sauer, I'm a cardiologist and clinical trialist at St. Luke's Mid-America Heart Institute in Kansas City, and I'll be introducing today's discussion, and also my co-moderator, Dr. Kavita Sharma.

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Andrew J. Sauer: As well as, Drs. Marat Fudim and Daniel Burkhoff. So, I'm gonna go ahead and turn it over to my colleagues to introduce themselves real quickly, and then we'll get started.

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Kavita Sharma: Thank you, Andrew, and welcome to our podcast today. I'm Kavita Sharma, Director of Heart Failure and Heart Transplantation at Johns Hopkins University. I also have a long-standing interest in HFpEF, and really thrilled to be here to co-moderate with you, Andrew, and with our esteemed guest speakers today. Thank you.

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00:01:15.530 --> 00:01:22.920
Dan Burkhoff: Hi, I'm Dan Burkhoff from the Cardiovascular Research Foundation. I am the Director of Heart Failure Hemodynamics.

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Dan Burkhoff: and mechanical circuitories support research at the Cardiovascular Research Foundation.

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Dan Burkhoff: And I'm really happy to be here to talk about this really interesting topic with you all.

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00:01:34.200 --> 00:01:42.729
Marat Fudim: And my name is Marat Fudim, I'm a heart failure cardiologist at Duke, and I run a remote monitoring clinic and device clinic, here at the institution.

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00:01:43.840 --> 00:01:56.119
Andrew J. Sauer: Well, it's great to have everybody here today. I also just want to point out to our audience that Dan Berkoff has been one of the pioneers that led to what's become a very successful meeting called THT.

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Andrew J. Sauer: Sponsored by CRF, and has really been a great place to accelerate conversations around technology and device-based therapies and heart failure.

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00:02:04.660 --> 00:02:22.369
Andrew J. Sauer: And Murat, kicked off, really the inaugural Heart Failure Devices, session coinciding with Heart Failure Society meeting this past year, which was a wild success. And, you know, that's a big part of why we were so fortunate, Kavita and I, to invite both of you here.

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Andrew J. Sauer: Because we're really going to take a quick tour over the next 30-35 minutes about the intersection of device-based therapies, remote monitoring, etc, as it relates to mildly reduced and preserved ejection fraction heart failure.

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00:02:35.920 --> 00:02:47.209
Andrew J. Sauer: Admittedly, I'll say up front that we recognize that many of what we're… of the topics we're going to be reviewing include some emerging, spaces, so not exactly

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Andrew J. Sauer: as standardized, if you will, as medical therapies, and certainly guideline-endorsed medical therapies. And we can point out, also, that the guidelines, the ACC, AHA guidelines.

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Andrew J. Sauer: Don't tell us a whole lot about device-based therapies, and we can maybe talk a little bit about some of those reasons, but…

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00:03:06.390 --> 00:03:21.320
Andrew J. Sauer: We are going to try to feature, device-based therapies that are featured in the guidelines, as well as some that are sort of emerging, FDA approved, and also maybe soon to be approved after further clinical trial investigation. So…

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00:03:21.330 --> 00:03:39.500
Andrew J. Sauer: I'm just gonna start by kicking the first question to my colleague, Kavita. And, you know, one of the things that comes up, Kavita, is that, you know, it feels like sometimes it's like an either-or when it comes to device-based therapies, and so there tend to be these,

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00:03:39.500 --> 00:03:59.399
Andrew J. Sauer: postures of, well, we gotta do meds, meds, meds, but there's some limitations to meds. We don't want to be disparaging meds, we've already talked about it on this podcast series, but where do you think about the role of device-based therapies in general for mildly reduced and preserved ejection fraction heart failure, just as kind of like an overview?

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00:04:00.300 --> 00:04:25.180
Kavita Sharma: Sure, thanks, Andrew. So, let's just maybe take even a step back before we consider, you know, medical therapy and device-based therapy, and just recognize where we are in HFpEF, certainly, today, compared to just even 8, 7, 8 years ago, where we had very, very limited guideline-directed medical therapy for this patient population. We all know the statistics. Over half of heart failure in the United States, patients with preserved EF,

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00:04:25.250 --> 00:04:50.239
Kavita Sharma: often with outcomes that are not different from HFrEF counterpart patients with heart failure, and a population that suffers from significant morbidity, day-to-day symptoms, symptom burden. And so, you know, it's wonderful that we now have what we call GDMT therapies that are available for this patient population, but I think those of us who see these patients regularly

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00:04:50.240 --> 00:04:52.849
Kavita Sharma: In clinical practice, we all recognize that

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00:04:52.850 --> 00:05:17.739
Kavita Sharma: you know, GDMT therapies, as great as they are, and with compelling evidence, do not necessarily treat all of the related symptoms and comorbidities that we see in this patient population, often with continued dyspnea, exercise intolerance, fatigue, and persistent congestion in spite of diuretic therapy and GDMT agents. And so, you know, from my standpoint as a clinician, and also someone who's been involved in

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00:05:17.740 --> 00:05:42.719
Kavita Sharma: trials over the years, I think we really, as a field, ought to be looking at device therapies as adjunct therapies, as therapies that are offered in parallel, as we study them more as they come into FDA approval and into the guidelines, and not an either-or approach, simply because we have a heterogeneous population, high symptom morbidity, and not every patient is sufficiently treated with

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00:05:42.720 --> 00:05:55.310
Kavita Sharma: GDMT therapies alone. I think we can agree to that. So that's sort of my 30,000-foot view of this. There's obviously nuances to who are the patients that are the right fit for each respective therapy, and hopefully we'll get into that over the next half an hour.

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00:05:56.690 --> 00:06:07.800
Andrew J. Sauer: Yeah, so as we kind of just dig into that a little bit more, you know, you see a lot of patients outside of just traditional HFPEF. You also are a transplant doc, and you intersect with

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00:06:07.800 --> 00:06:25.220
Andrew J. Sauer: other pathophysiology states, but can you give us, like, a quick snippet of, like, what are the red flags to make you think about as it relates to… this isn't exactly just your general run-of-the-mill HFPEF, but this may be something different. Is there a checklist you follow, or something to make sure that we're focused on true

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00:06:25.340 --> 00:06:30.489
Andrew J. Sauer: HFpEF, or how do you sort of differentiate that from other potential masqueraders?

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Kavita Sharma: Sure, that's a great point, and so the guideline definitions of HFPEF are quite broad, certainly in the American guidelines. Clinical signs and symptoms of heart failure, it is a clinical diagnosis, ejection fraction 50% or greater, and maybe some evidence of elevated left ventricular and diastolic filling pressure, whether that's elevated NTPro BNP or hemodynamic or echocardiographic markers.

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Kavita Sharma: But we know that that's still relatively broad, and there are other diagnoses that can sort of fit those definitions, but aren't our garden variety HFpEF. And the things that I think are important to rule out, so to speak, as you've said, is, you know, infiltrative cardiomyopathy, so amyloidosis, for example, especially in the current era with so many targeted therapies for TTR amyloidosis and for AL amyloidosis.

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00:07:20.210 --> 00:07:45.169
Kavita Sharma: Clinical clues there might be the patient who presents without the usual, comorbidities or risk factors for HFPEF, with the predominant phenotype today, cardiometabolic or obesity-associated HFPEF. So that leaner patient, low blood pressure profile, elevated biomarkers like troponin and NTPro-BNP, that's a yellow to red flag for maybe being another entity, and it needs to be evaluated.

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00:07:45.170 --> 00:08:08.739
Kavita Sharma: We also want to think about inflammatory cardiomyopathies, so younger patients, again, without that comorbidity profile, without those risk factors, maybe preceding clinical history for an inflammatory process or extracardiac disease that would support that. And then, of course, we have valvular pathologies, but in fact, you know, we will talk about some of those valvular pathologies today, and that maybe we are now starting to see more and more of an overlap, or

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00:08:08.740 --> 00:08:27.920
Kavita Sharma: intersection between HFpEF physiology and valvular pathophysiology, and how do we approach treatment of the underlying valvular disease in addition to HFpEF. But infiltrative and inflammatory, as well as hereditary cardiomyopathies definitely are up there to rule out and take a slightly different approach that targets those

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00:08:27.920 --> 00:08:29.620
Kavita Sharma: Those, phenotypes.

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Andrew J. Sauer: Yeah, I love that point of view. And so, Dan, you know, you are our kind of hemodynamic guru. A lot of us have been learning from you.

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00:08:38.789 --> 00:08:57.359
Andrew J. Sauer: for many years. I go back to my fellowship, my first exposure to you. I was very fond of your Harvey app, for example, where you, you know, gave us a very practical way to explore pressure volume loops. So, what do you want to tell us about what we kind of understand about

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00:08:57.920 --> 00:09:01.450
Andrew J. Sauer: hemodynamically oriented phenotyping of heft

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Andrew J. Sauer: versus mildly reduced or reduced ejection fraction heart failure. You know, what are the kind of take-home points that we need to think about as we try to establish, sort of, what type of patient we're talking about when they have HFpEF.

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00:09:15.770 --> 00:09:16.400
Dan Burkhoff: Sure.

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00:09:16.500 --> 00:09:18.839
Dan Burkhoff: Yeah, thanks for that question.

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00:09:18.850 --> 00:09:35.319
Dan Burkhoff: I really think that, there are a lot of commonalities between heart failure across the spectrum of ejection fractions in terms of hemodynamics. And obviously, you know, in the current era, the thing… the one main thing that differentiates

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Dan Burkhoff: them is the ejection fraction, which is very easy to measure, and so you can neatly put these patients into, you know, EF categories.

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00:09:44.180 --> 00:09:58.469
Dan Burkhoff: Now, I do think that, you know, there has been a lot of emphasis on hemodynamic characterization of heart failure preserved ejection fraction as a means of making the diagnosis definitive when it's less clear.

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00:09:58.590 --> 00:10:18.359
Dan Burkhoff: And as you know, in some of the diagnostic algorithms, you know, invasive hemodynamics and exercise testing is the last thing that you do if it's an unclear diagnosis. And what do you see? When you test these patients, you see a very rapid and marked

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00:10:18.370 --> 00:10:30.830
Dan Burkhoff: elevation of pulmonary capillary wedge pressure. They are… these patients are intolerant to, even a volume challenge by raising the legs, and within one minute.

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00:10:30.830 --> 00:10:40.690
Dan Burkhoff: Of exercise, you can see the pulmonary capillary wedge pressure increase, you know, to over 30, 35 millimeters of mercury.

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Dan Burkhoff: And the first thing I would say is that it's not just the wedge pressure that goes up. The CVP goes up in the same proportion, as the wedge pressure in every study that we've, that we've looked at both… at both parameters. So, that really has led us to really understand what is it

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00:11:00.560 --> 00:11:12.820
Dan Burkhoff: to question, what is it about HFPEF that these patients are not able to, you know, to tolerate volume load? And where is the volume coming from? When you exercise, it's really, we think.

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00:11:12.820 --> 00:11:23.599
Dan Burkhoff: Is that it is, number one, they are volume overloaded to start with, and if you look at any measure of estimate of total plasma volume.

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Dan Burkhoff: It's elevated, and not only that, when they exercise, the shifting of the volume from the unstressed to what we call the stressed blood volume is exaggerated in HFPEF patients.

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00:11:37.800 --> 00:11:42.759
Dan Burkhoff: And that results in an increase in both the wedge and the CVP.

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00:11:42.940 --> 00:11:45.850
Dan Burkhoff: Now, is this unique to HFpEF?

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Dan Burkhoff: Do you see this in mildly reduced or reduced ejection fraction? Well, usually you do see the same things in heart failure across the spectrum. It has a spectrum of ejection fraction. It has just been

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00:12:01.380 --> 00:12:09.349
Dan Burkhoff: That, traditionally, we have not looked at exercise testing hemodynamics in heart failure reduced ejection fraction.

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Dan Burkhoff: It was not required for us to make the diagnosis. It had not become part of our unders… of our… the requirement to develop devices or… or drugs. And really, I believe, I think that… that, you know, the… the emphasis on hemodynamic testing

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00:12:28.670 --> 00:12:43.350
Dan Burkhoff: in HFpEF is, is really… was driven by the observations in the early, you know, 2010s by, you know, a lot by Barry Borlaug, and before that, Delane Kitzman, you know, showing what happens to pressures.

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00:12:43.370 --> 00:12:54.750
Dan Burkhoff: In those patients to help make the diagnosis. But I do think there are a lot of commonalities across the spectrum of ejection fractions in the response to, to exercise.

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00:12:59.240 --> 00:13:03.529
Andrew J. Sauer: Yeah, thanks for that overview. I think that's a great segue to…

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00:13:03.630 --> 00:13:16.499
Andrew J. Sauer: kind of bring us into how do we incorporate hemodynamics into remote hemodynamic monitoring. So Murat, you direct your remote monitoring program, and as it intersects with device-based therapies at Duke.

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Andrew J. Sauer: How are you thinking about the landscape of remote PA pressure monitoring as a tool, especially as a tool uniquely suited for patients with mildly reduced or preserved ejection fraction heart failure?

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00:13:30.340 --> 00:13:46.129
Marat Fudim: Yeah. Before I jump into that, let me just address what just Dan said. I think in clinical practice, hemodynamic testing, including, you know, doing it longitudinally, that's where RPM comes in, you're sort of committing to measuring pressures longitudinally, or whatever other metrics you might be measuring.

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00:13:46.340 --> 00:14:03.499
Marat Fudim: But when we do it cross-sectionally in clinical practice, the relevance of human dynamic testing, I think, is becoming greater, because the problem that we see in clinical practice is that the presence of diastolic dysfunction, some of those things that Kavita mentioned, that might be present that indicate heart failure as being, you know, at least being a consideration.

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00:14:03.570 --> 00:14:14.460
Marat Fudim: But we have a lot of mimickers, and that's real. I mean, obesity, a lot of comorbid diseases, like lung disease, anemia, they can't present itself like heart failure, and distinguishing those components

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Marat Fudim: Becomes tricky, and hemodynamics tend to be often be… often tend to become the deal breaker.

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00:14:19.790 --> 00:14:38.870
Marat Fudim: to tell you, you know, is this actually primarily driven by cardiovascular disease or non-cardiovascular disease, when you see what the symptoms are and how they overlap with the severity of human dynamic testing? And I think that's where exercise really comes in, because that gives you a lot of extra data points to tell you what might be actually driving the symptoms.

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00:14:38.940 --> 00:14:44.849
Marat Fudim: So, with that in mind, because hemodynamics tend to be the gold standard to say.

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00:14:44.880 --> 00:15:02.690
Marat Fudim: congestion is present and or, the heart being stiff and or weakened is driving the symptoms, it is natural to then say, well, human dynamics could also be used longitudinally to track congestion and could be used for two purposes. I mean, one purpose is

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00:15:02.690 --> 00:15:08.209
Marat Fudim: something's going the wrong way, I call it a red flag, you know, the pressures are going up, actions needed.

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00:15:08.570 --> 00:15:19.579
Marat Fudim: But it might not necessarily be that the action is titration of medications, and in many cases, we just identify the risk being high, call the patients in, and try to correct whatever might be going on.

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00:15:19.740 --> 00:15:24.039
Marat Fudim: That is driving the pressures to go the wrong way.

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00:15:24.180 --> 00:15:27.339
Marat Fudim: And then the second way we like to think about hemodynamic

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Marat Fudim: testing is, longitudinal as part of RPM,

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00:15:31.050 --> 00:15:50.670
Marat Fudim: is, of course, that any derangement could also be used to titrate medications, which, you know, is the holy grail, is that we could actually titrate medications based on remote signals that would avoid the patients who have to come in, us be having to see them in person. We could maybe even unleash robots on patients, software that could titrate medications.

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00:15:50.670 --> 00:15:57.979
Marat Fudim: based on, digital input, remote sensor input. But I think the world is a little bit too complicated right now.

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Marat Fudim: to allow us to do a lot of titration of medications based on RPM signals, and in many cases, unfortunately.

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00:16:06.450 --> 00:16:19.019
Marat Fudim: RPM comes down to being a red flag, where we really just identify there might be a problem, and then have to sort of sort out what the problem is, and it does result in us often having to call and talk to patients and see them in person.

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00:16:19.180 --> 00:16:29.480
Marat Fudim: Now, I think to your question, you know, what solutions out there, there's a lot of solutions. I think the gold standard is in implantable solutions, such as the CardioMEMS and the Cordella's of this world. There's a lot of them in the making.

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Marat Fudim: that are gonna target other areas besides just the PA pressures, and there's a whole slew of

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Marat Fudim: hemodynamic sensors that are seeking to reproduce and measure human dynamics.

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Marat Fudim: But doing that non-invasively through patches or point-of-care devices, and to collect other biometrics that could mimic pressure signals or other multi-organ system

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00:16:52.630 --> 00:17:06.589
Marat Fudim: signs that you can derive from light sensors, vibrations, ECGs, so I do think that our world of remote sensors is becoming dramatically larger as we… as the engineering world really is learning

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00:17:06.829 --> 00:17:15.530
Marat Fudim: How to, you know, derive a lot of deep insights from non-invasive and invasive sensors, and deploy them minimally invasively.

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00:17:21.050 --> 00:17:31.729
Andrew J. Sauer: Yeah, I think, what also I think has been a challenge with hemodynamic monitoring has been that we focused a lot on the monitoring and not on the management, and I think the best programs out there

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00:17:31.900 --> 00:17:43.669
Andrew J. Sauer: We have figured out a way to make that a… not just a semantic change, but really a strategy where we use the congestion signals that you described to trigger

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00:17:43.670 --> 00:18:03.400
Andrew J. Sauer: changes to therapies, and then we bring back to our medical toolbox. We have great therapies that are decongestive in nature, but are also part of GDMT, and so you make sure that patient is on those therapies while also adjusting, potentially, their diuretics. I do think that we also discover, with a lot of these patients.

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00:18:03.440 --> 00:18:16.220
Andrew J. Sauer: that they may have concomitant, structural, lesions, valve disease. So, you know, Kavita, maybe you can kind of just give us a frame of reference about how you think about

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00:18:16.240 --> 00:18:25.869
Andrew J. Sauer: the order of events, because we can see a lot of patients who are described to us as HFpEF, and then we go and look, listen to them, and we hear that kind of mid-peaking, maybe late-peaking.

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00:18:25.870 --> 00:18:39.419
Andrew J. Sauer: murmur, you know, their A2 is going away, their P2 is getting kind of loud. This is getting suspicious, and then we go take another look at the echo, and we find, you know, they've got a lot more AS, aortic stenosis, than maybe people are fully appreciating, so…

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Andrew J. Sauer: They also have MR, they also have TR, so how do you think about approaching that kind of complexity?

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Kavita Sharma: Yeah, that's a great question, Andrew, and, you know, I'm not sure I have the exact, you know, perfect answer to it. There are many different ways to do this, but I, you know, I couldn't agree more with Dan and Marat on the importance of hemodynamic characterization in HFPEF, but of course, we have to be realistic about

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00:19:02.490 --> 00:19:25.550
Kavita Sharma: availability of invasive hemodynamic testing, around the experience with this sort of higher-level testing, and really what is out there for clinicians in the community. And so, really, it starts with non-invasive assessment. I think just the clinical history, the trajectory, the symptomatology of predominantly right-sided, left-sided symptoms, and then really

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00:19:25.550 --> 00:19:50.469
Kavita Sharma: having a good look at the echocardiogram to start. In some cases, TEE if needed, which is still going to be more readily available than invasive right heart catheterization at many places. But again, a low threshold to, if needed, to either refer out or, if internally available, to perform exercise hemodynamic testing. Now, at Hopkins, certainly, we're very biased to invasive right heart catheterization. We do supine

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Kavita Sharma: bicycle exercise, but other places have different other strategies to, really kind of induce

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Kavita Sharma: revocable exercise and changes in the hemodynamic state, but I think it starts with the clinical course of the patient, and then the non-invasive assessment to begin with, with a close look at the valves. Now, there's always, as with HFrEF, a chicken or egg phenomenon. Is it the HFpEF that's driving what's being seen, maybe related to the valves, or vice versa?

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00:20:17.020 --> 00:20:33.580
Kavita Sharma: Some patients will, of course, have underlying pathology, rheumatic heart disease, other things that might predispose them to valvular heart disease, but barring those, you know, situations, I think there will always be that question of chicken versus egg here. But to me, it starts with clinical assessment and non-invasive first.

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00:20:35.800 --> 00:20:37.930
Andrew J. Sauer: Yeah, and how do you,

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Andrew J. Sauer: kind of tackle the question, and maybe I'll… I'll pitch it to you, Murat. How do you tackle the question about

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00:20:46.360 --> 00:20:58.820
Andrew J. Sauer: okay, how much of this is that we need to fix the valve lesion, and how much of this is that we need to do a better job with other forms of optimization? And that doesn't have to just be meds, by the way. You know, I'm thinking of

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00:20:58.820 --> 00:21:14.149
Andrew J. Sauer: mitral regurgitation cases that we've all seen, and maybe also tricuspid regurgitation. How do you think about approaching that from the heart failure clinician perspective as we work to support our structural interventional colleagues?

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00:21:15.130 --> 00:21:35.090
Marat Fudim: Oh, I love that question. So, I think in the setting of AS, an obstructive lesion, you tend to have to tackle that, and heart failure is sort of a concomitant problem, chicken or egg, it doesn't matter. You sort of have to tackle the obstruction. In the regurgitant lesions, it becomes much more nebulous as to what is the primary, what's the secondary cause.

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Marat Fudim: Aka in the MR or TR,

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00:21:38.910 --> 00:21:48.469
Marat Fudim: And I would say that we keep going through this battle, and I think from a heart failure standpoint, we are readily to acknowledge that you probably should never ignore the underlying cardiomyopathy.

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Marat Fudim: that has contributed or resulted from the MR and TR, so it doesn't matter what came first, the reality is that you have myopathy. The heart is no longer normal, structured abnormal, electrically abnormal.

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00:22:01.280 --> 00:22:02.270
Marat Fudim: And…

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00:22:02.680 --> 00:22:19.390
Marat Fudim: providing the background therapy of MR… of myocardial therapy, such as GDMT, will always be true. So I don't think that anybody will be harmed by providing GDMT in a setting of, you know, mild, moderate, severe MRTR. Now, then the much harder question would be.

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00:22:19.390 --> 00:22:23.630
Marat Fudim: is on top of GDMT that can be implemented in a matter of weeks to months.

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Marat Fudim: is the structural intervention going to result in an improvement? And I think that's where trials comes in, right? And the trials tell us, at least in a MR space, for sure.

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00:22:33.360 --> 00:22:37.460
Marat Fudim: There's symptomatic benefit, and there's a benefit on morbidity and mortality.

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00:22:37.690 --> 00:22:39.989
Marat Fudim: There's now a series of trials to suggest that.

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Marat Fudim: and, you know, U.S. and European trials. I think in the TR space, the jury is a little bit out. We know it certainly symptomatically improves upon patients' status, and we hopefully will have more evidence in the future to demonstrate that that all then extends to rehospitalization burden as well. So I do think that

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00:22:57.610 --> 00:23:10.319
Marat Fudim: Those are complementary, and where our job is secure is to then be able to say, now is the time to trigger the structural intervention, and that will be, no doubt, always be a discussion between the different teams.

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00:23:10.330 --> 00:23:23.209
Marat Fudim: I don't know that we communicate with each other well enough. I think often you see, you know, structural interventions maybe moving ahead without having input from heart failure. That's in clinical trials that have done it very, very, carefully.

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00:23:23.250 --> 00:23:37.059
Marat Fudim: such as the co-op trial, you actually had to have a heart failure investigator and a structural investigator both sign off in individual visits prior to proceeding with an intervention. Now, I don't know if this clinical practice goes exactly that the same way, but,

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00:23:37.370 --> 00:23:43.379
Marat Fudim: that… I think those Valve teams will only get more and more elaborate going forward, because

there's more and more solutions coming on the market.

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00:23:45.160 --> 00:24:04.239
Andrew J. Sauer: Yeah, I think that's a really key point. You know, we ultimately have to remember that heart failure clinicians have always been part of these workflows for these structural interventions, particularly regurgitant lesions, as you point out, in the clinical trials. I was a member of the Medical Optimization Committee, for example, for Triluminate.

116
00:24:04.240 --> 00:24:20.280
Andrew J. Sauer: And people forget very quickly that every single patient for, presenting for evaluation for tricuspid intervention in that study was required to have a right heart catheterization, was required to have a hemodynamic study.

117
00:24:20.280 --> 00:24:35.049
Andrew J. Sauer: And it was our job to make sure that the PA pressures were, from a left-sided heart failure disease standpoint, were optimized. And what we also discovered is that this population was highly enriched with good old-fashioned, run-of-the-mill

118
00:24:35.050 --> 00:24:37.020
Andrew J. Sauer: Preserved ejection fraction heart failure.

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00:24:37.020 --> 00:25:01.330
Andrew J. Sauer: They made up the bulk of the population, and many of these patients, as you would not be surprised, when given better optimization of their medical therapies, which could include, you know, just, you know, adding an SGLT2 inhibitor, for example, their PA pressures came down, and when we re-looked at their tricuspid valve, they did not have significant tricuspid regurgitation anymore. So, it's a really key point that we can't just focus on

120
00:25:01.420 --> 00:25:06.620
Andrew J. Sauer: You know, treating the valve lesion, but also treating the underlying cardiac disease.

121
00:25:12.250 --> 00:25:15.189
Andrew J. Sauer: I don't know, Kavita, did you want to lead us into neuromodulation?

122
00:25:15.190 --> 00:25:30.930
Kavita Sharma: Yeah, let's segue to the next, sort of, subtopic here. So, we wanted to chat with, with all of you about an emerging area and concept regarding neuromodulation and contractility-adjacent devices. How do we approach this

123
00:25:30.930 --> 00:25:38.480
Kavita Sharma: field that's growing rapidly in our HFpEF population, so maybe we can begin with,

124
00:25:38.730 --> 00:26:01.029
Kavita Sharma: patient profile, how do we identify the right patients for these therapies, and then what are the therapies that are currently, you know, that we know much about, that are coming down the pipeline? And so, Dan, maybe you can kick us off with, conceptually, you know, what is this area? How might we see this in the future? And HFPEF, and then Marat can maybe tell us a little bit about patient selection and how

to phenotype for the right

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00:26:01.220 --> 00:26:02.280
Kavita Sharma: Candidates.

126
00:26:02.280 --> 00:26:02.940
Dan Burkhoff: Sure.

127
00:26:03.070 --> 00:26:08.630
Dan Burkhoff: You know, devices for heart failure, really…

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00:26:08.780 --> 00:26:17.779
Dan Burkhoff: Their history started in the late 80s, early 1990s, really focused on heart failure reduced ejection fraction.

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00:26:17.960 --> 00:26:28.839
Dan Burkhoff: And really, it's only been in the last 15 years or so that devices, the concept of using devices in HFPEF, really has emerged.

130
00:26:28.960 --> 00:26:44.570
Dan Burkhoff: And along the way, along the last 15 years, there have been several, you know, several different classes of devices, and the first one was the interatrial shunts. If I, you know, if we… let's put the remote patient monitoring to the side.

131
00:26:44.570 --> 00:26:58.560
Dan Burkhoff: Because that, you know, that is really, you know, universal across, across, ejection fractions, addressing the volume overload. The shunts, interatrial shunts were really the first device, and as you all probably appreciate now.

132
00:26:58.560 --> 00:27:15.699
Dan Burkhoff: Their, their fate is kind of up in the air right now. There are… there have been two failed clinical trials with shunts. One that was specifically in patients with HFPEF, and the other which had a broader, a broader inclusion of both HFREF and HFPEF.

133
00:27:15.810 --> 00:27:20.040
Dan Burkhoff: The HFPEF study identified… that was negative, identified a subgroup.

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00:27:20.070 --> 00:27:27.829
Dan Burkhoff: That, seem to benefit, and that is a… that study, the confirmatory study in that subgroup population is ongoing.

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00:27:27.840 --> 00:27:43.640
Dan Burkhoff: The, the device, the, the study that, that looked at, shunts across the range of ejection fractions, it was negative in the HFPEF population and positive, if you will, suggested for positive in the HFREF population.

136
00:27:43.700 --> 00:27:56.729
Dan Burkhoff: However, the HFpEF population really fit with the non-responder group that was identified in the first study that I mentioned. So, the fate of the shunts is a little bit up in the air.

137
00:27:56.820 --> 00:27:59.310
Dan Burkhoff: Especially as it relates to HFpEF.

138
00:27:59.490 --> 00:28:14.580
Dan Burkhoff: There are other, therapies that, have also emerged first, being studied in HFrEF, and these are the barostimulation, therapies and cardiac contractility modulation.

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00:28:14.610 --> 00:28:22.830
Dan Burkhoff: Again, these, both have been studied relatively extensively in the HFREF population, and now are expanding.

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00:28:22.880 --> 00:28:28.459
Dan Burkhoff: To the higher ejection fraction. CCM, cardiac contractility modulation, in fact.

141
00:28:28.570 --> 00:28:33.289
Dan Burkhoff: is approved for patients with EFs from up to 45%.

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00:28:33.470 --> 00:28:41.509
Dan Burkhoff: And that was really an observation. It was not expected, but it was an observation that was made early on.

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00:28:41.740 --> 00:28:48.610
Dan Burkhoff: And, and now there is a study ongoing with CCM in patients with EFs up to 60%.

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00:28:48.780 --> 00:29:03.249
Dan Burkhoff: So, that study is ongoing, and, similarly for the baro reflex, there are, you know, there are studies that are, that are going to look into, this. And this really, really gets at the concept that

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00:29:03.260 --> 00:29:15.299
Dan Burkhoff: You know, in all forms of heart failure, there is some degree of, some degree of, of, sympathetic activation that, that needs to be dealt with.

146
00:29:15.360 --> 00:29:33.950
Dan Burkhoff: And more directly, you know, there has been… there have been studies that are looking at denervation platforms that are now emerging. There was originally the renal denervation, which was developed for heart failure originally, very quickly switched to hypertension.

147
00:29:34.020 --> 00:29:42.370
Dan Burkhoff: Is approved for hypertension now, and still is being studied, in small degrees for, for, heart failure.

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00:29:42.400 --> 00:30:01.019
Dan Burkhoff: But now we've got the splenic nerve denervation, which is directly addressing this… the concept that during exercise, the splenic… the splenic venoconstriction that's mediated by the greater splenic nerve and the nervous system

149
00:30:01.020 --> 00:30:16.380
Dan Burkhoff: is really responsible, in large part, for this massive shift of blood from the splenic bed to the central location that results in both the increase in both CVP and wedge.

150
00:30:16.850 --> 00:30:22.259
Dan Burkhoff: And also, even more recently, is the pulmonary artery denervation.

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00:30:22.300 --> 00:30:40.880
Dan Burkhoff: This is focused on patients with pH HFPEF at this point, but I really believe that the cardiac plexus and the plexus of nerves around the pulmonary arteries is doing more than just affecting the pulmonary bed.

152
00:30:40.930 --> 00:30:49.209
Dan Burkhoff: And so I think that we're going to see, a lot of things that are going to emerge from these studies that are really, really just getting going.

153
00:30:49.330 --> 00:31:06.170
Kavita Sharma: Yeah, thank you. That's such a great, succinct overview of the landscape of these therapies. Murat, in the last couple of minutes that we have, maybe I'll ask you, as both a clinician and a clinical trialist in this space, what are we really getting at? What are the practical, sort of.

154
00:31:06.170 --> 00:31:17.700
Kavita Sharma: outcomes that we're trying to improve with these therapies, and how should we be looking at these therapies in terms of patient response, so to speak. It's a broad question, but maybe you can share some thoughts on this.

155
00:31:18.120 --> 00:31:20.529
Marat Fudim: And that's in regards to the novel therapies?

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00:31:20.530 --> 00:31:21.320
Kavita Sharma: Yes, exactly.

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00:31:21.320 --> 00:31:31.809
Marat Fudim: discussed? Yeah. Well, I think I will take a step back, because what is interesting with device-based therapies, and I have a lot of them that we are testing in our institution.

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00:31:32.060 --> 00:31:38.700
Marat Fudim: Is that device-based therapies, because they tend to be a one-shot or implantable, they tend to be high upfront risk.

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00:31:38.950 --> 00:31:52.569
Marat Fudim: But they require, unlike the drugs, for some reason that we always think, you know, you can always stop drugs, so if you have a side effect where they don't benefit you, you can stop. But device-based solutions tend to be a lot harder because you're sort of committed to the pathway.

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00:31:52.620 --> 00:32:05.509
Marat Fudim: So with device-based therapies, what the trend is that's emerging is we do a lot deeper phenotyping with device-based solutions before we commit to them, before we either randomize patients to it or we prescribe the therapy.

161
00:32:05.570 --> 00:32:15.620
Marat Fudim: And that, in my opinion, is a good thing because it forces us to uncover the true presence of heart failure preserved ejection fraction. Often, these studies actually demand that you do exercise hemodynamics.

162
00:32:15.830 --> 00:32:33.300
Marat Fudim: the demanded to determine some form of additional physiological signs that support that heart failure is really what's driving the signs and symptoms. They have actually a longer list of I&E criteria, inclusion-exclusion criteria, than we often use to from drug trials. So, I think it's just,

163
00:32:33.460 --> 00:32:46.099
Marat Fudim: The need to deep phenotype ahead of the solutions is what will make these therapies in the long run more successful, but at the same time makes the applicable patient pool a lot smaller.

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00:32:46.740 --> 00:32:56.509
Marat Fudim: And, but I will, though, say that, you know, only results will matter at the end of the day, and these device-based solutions

165
00:32:56.970 --> 00:33:04.430
Marat Fudim: while costly and slow to be implemented, they will need to deliver on, you know, the promise of the

166
00:33:04.530 --> 00:33:17.480
Marat Fudim: strong slash hard outcomes, such as the rehospitalization and death. The only problem is in the small numbers that they're getting often done, they will not be able to do that anytime soon, because they often aim to improve on quality of life, because the size of these studies is

167
00:33:17.480 --> 00:33:30.309
Marat Fudim: you know, in the dozens to hundreds of patients, not in thousands. So it's a little bit of an interesting space we're in, and hopefully we'll find ways to, you know, do minimally invasive procedures in larger scale, so we can test them in larger scale as well.

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00:33:31.400 --> 00:33:35.390
Kavita Sharma: Thank you, Marat, that was great. I'll send it back to you, Andrew, to wrap up.

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00:33:35.440 --> 00:33:53.529
Andrew J. Sauer: Yeah, I was just gonna say, I just… it's amazing how much time flies and how much

ground we've covered, which, obviously, so much of what we talked about today is really probably just a teaser for our audience, and I think, I would just encourage our audience to continue to participate in the conversations that we have.

170
00:33:53.570 --> 00:34:03.710
Andrew J. Sauer: at a lot of these emerging meetings that I've referenced, where there's a lot more intentional focus on the intersection of heart failure with device-based therapies. And I'll probably just try to sum up

171
00:34:03.740 --> 00:34:19.359
Andrew J. Sauer: You know, what we've talked about today is really making sure that you do a thorough work up front when seeing your patient to make sure you understand that patient's particular sort of phenotype as it relates to their disease.

172
00:34:19.360 --> 00:34:37.929
Andrew J. Sauer: Think carefully about the hemodynamic evaluation, think about aggressive hemodynamic evaluation diagnostically up front, and even potentially considering that in a remote, in a remote monitoring capacity for particular patients who look like the patients who are in our clinical trials.

173
00:34:37.929 --> 00:34:46.469
Andrew J. Sauer: of those studies. Recognize that there are masqueraders, and that we need to make sure we've excluded those before we treat patients.

174
00:34:46.469 --> 00:35:02.770
Andrew J. Sauer: With just medicines, and as we're starting to explore device-based therapies, recognizing that one of the other categories of masqueraders can just be, common valve disease that is associated with our particularly elderly population.

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00:35:02.770 --> 00:35:13.299
Andrew J. Sauer: And that we need to work with our partners in the structural and interventional space to make sure that we've done our best with medications and other interventions

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00:35:13.300 --> 00:35:28.440
Andrew J. Sauer: Before we commit to valve replacement or valve interventions, but that… those are oftentimes necessary as part of good therapies for true cardiomyopathy or related to heart failure with preserved or mildly reduced ejection fraction.

177
00:35:28.520 --> 00:35:45.859
Andrew J. Sauer: And lastly, we just heard a great tour of a number of existing device-based therapies. Recently, FDA-approved device-based therapies, such as cardiac contractility modulation, which actually has a national coverage determination.

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00:35:45.860 --> 00:35:57.789
Andrew J. Sauer: And is expanding, as you heard, into higher ejection fraction, heart failure. But also, stay tuned for what's coming with many of these other device-based therapies, because I do think it's an exciting time in our field.

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00:35:57.790 --> 00:36:16.060
Andrew J. Sauer: To really think about how to be a comprehensive clinician taking care of these patients, and once again, not thinking about therapies as either meds or devices, but really in a complementary fashion, because we can do a lot better for our patients if we have the full menu

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00:36:16.060 --> 00:36:18.160
Andrew J. Sauer: Of therapeutic options in front of them.

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00:36:18.370 --> 00:36:29.169
Andrew J. Sauer: And so with that, thank you again for joining us for this conversation, and just as a reminder that this is an episode as part of the American Heart Association's Heart Failure Podcast Series.

182
00:36:29.170 --> 00:36:40.910
Andrew J. Sauer: And more episodes can be found at LearnHeart.org, and this is a really, we're really grateful to the audience for joining us on our series, and I just want to thank my colleagues for joining us today.

183
00:36:43.300 --> 00:36:44.300
Marat Fudim: Thanks for having us.

184
00:36:44.700 --> 00:36:45.429
Kavita Sharma: Thank you.

185
00:36:46.180 --> 00:36:46.870
Dan Burkhoff: Thank you.