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Panel: Issues Dealing with Left Heart Disease in PH

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Dr. McLaughlin:
So those were all really great talks of a very common problem. I'm going to ask more of a population health-type question, and more of a practice management-type question. You know, as a PH doc, you know, probably 8 out of 10 patients that I see are group 2 due to diastolic heart failure and so, you know, that's a lot of volume for us to manage and it can delay patients with group 1 PAH being seen in a timely fashion. And on the heart failure side, you know, our heart failure docs are inundated with patients, many of them really want to focus on advanced therapies, and the numbers are staggering at 30 million people. And there seems to be an underappreciation of this particular problem in the community of primary care docs. So, the way I see is like, this is not sustainable, and you know, causing problems on both sides. So, just in terms of population health management/practice management, do you guys have any thoughts on what we should be doing differently as a healthcare system? I know it's the easiest question of the day, right?

Dr. Patel:
It's a big issue because HFpEF is only going to become more common. It's outstripped HFrEF as the most common type of heart failure, and these patients are everywhere, they're in every clinic. And, you know, I think that from a cardiology perspective, general cardiologists have to be able to manage HFpEF because there is just too much of a demand to see these patients, and it's out the door in terms of, you know, kind of wait times to see an advanced heart failure doctor, to see these patients. And there are therapies that we as a community, and the general cardiologists must become more comfortable starting that were traditionally maybe medications that we did not start in clinic, in general cardiology clinics.

But, you know, we have to step outside of our comfort zone with these medications, GLP-1 receptor agonists, SGLT2 inhibitors, because we're delaying care in our patients. They're getting rehospitalized and rehospitalized and they're suffering from high risk. And so, you know, I think that's a very important point. And I would just say, you know, historically, cardiologists have shown we can do this. You know, typically, you know lipids were viewed as an endocrinology disorder for a long period of time and, you know, we routinely prescribed statins, we routinely prescribed lipid-lowering therapies as cardiologists, general cardiologists, and whatnot, so it's just a matter of kind of keeping that message going that we can do this in the general clinic setting. And otherwise, you know, I don't have other good answers.

Dr. Cascino:
So, a few things that I would add is that I think it is an opportunity for multidisciplinary disease management as well. I think that there's a massive role here for pharmacist-led interventions going forward in the future. Clearly, we're at a point where we need to work together with, you know, everyone who is referring patients to work on education. And then, you know, down the line you could imagine things like artificial intelligence with echos is I think one area where there is some particular promise, where you could help use that to more

appropriately triage people. But, as someone who takes care of heart failure patients and also takes care of pulmonary hypertension patients, most of the time I'm just happy that they've gotten into my clinic because now I can lead them to the right place. Now, it is delays in care, it's not ideal and it's not the most efficient system, but at least they're in and we can get them started and get them to the right place.

Dr. Raza:
Yeah. I'll just echo what, you know, Ravi and Tom were saying. So, I also take care of heart failure patients as well as PH patients, and I think as Mike had alluded to earlier, and then as you just mentioned with especially leveraging AI, just really using the echo report. Even like changing how we report instead of just saying PASP estimated is elevated, pulmonary hypertension is mild, moderate, severe, or not there, what do we think is that likely underlying? Like, Do we think there's, you know, left heart disease prominence? Like, how else can we modify that report to really triage them? so that patient I presented in a case here for this section, I ultimately, you know, referred to Ravi for the HFpEF clinic, so how can we get them to Ravi? Or do they actually have amyloid? Tom talked about not missing any of those zebras. So, is there evidence of amyloid, for example on strain imaging, or hypertrophic cardiomyopathy on strain imaging? There's a lot of wealth of data that we can get from the echo, and from there really try to steer our patients in the right direction. And then I totally agree with what Ravi said about being more comfortable with prescribing therapies that we didn't necessarily used to think was our domain. So, really just the magnitude effect of SGLT2 inhibitors and then, we have a lifestyle medicine program at Northwestern, as I'm sure there's similar at a lot of institutions, but there's a waiting list that can sometimes be a year. And, so, waiting that amount of time to get patients to a bariatric surgical intervention program or to a GLP-1 agonist just doesn't seem reasonable. So, getting comfortable with that. And then even at the advent of things like finerenone, a lot of HFpEF patients who have CKD, hypertension, and so, being comfortable with other therapies. And even if we're not starting it, sending a letter back to the PCP referring and saying these are some of my suggestions while they're waiting to get to the next specialist.

Dr. McLaughlin:
Yeah. So, those are all really great thoughts. Another challenging question I have is, you know, we see this problem commonly, right, and yes, isolated post-capillary is the most common cause, but we think there's a lot of combined pre- and post-capillary, yet when we try to enroll these patients in clinical trials, we don't do a very good job, right. You know, there's so many clinical trials that have not enrolled, even CADENCE, you know, everyone is so excited at sotatercept and the enrollment in that is really, really poor. So, why do you think that is? You know, why are we having such a hard time studying these patients?

Dr. Patel:
You know, I think some of it is, you know, where you look. And so, it's a patient population that, for example, in many cardiology clinics we see we are just potentially not doing the same diagnostic tests that, let's say, they come to your clinic, and you know, you have made sure we've looked through invasive hemodynamics. A lot of these patients will get an echo, they'll get started on therapies, we don't know their true invasive hemodynamic physiology at rest and stress to say look, this is a high-risk patient with, you know, combined pre-/post-capillary PH. So, they kind of float around in the ether. They may get some therapies, but they don't get necessarily identified because of maybe the lack of willingness to do some of the invasive hemodynamic testing that we should do. You know, I think that at least from as a HFpEF clinic trialist in enrolling, it has become a little bit of a challenge with the past 2 years getting people on therapies that I know will reduce their risk of heart failure hospitalization and improve their quality of life. It does take some time. SGLT2 inhibitors, GLP-1, that occasionally delays enrollment into clinical trials and sometimes there're inclusion and exclusion criteria based on the timing of initiation of these therapies before enrollment in a new clinical trial, and it's important to give these patients the ability to try these medications.

Obviously, cost is an issue and tolerance is an issue, so not everyone will, one, benefit from them from a quality-of-life perspective, and two, be able to either afford them or tolerate them without side effects. So, I think that's created some challenges as well in getting them into these trials, which, you know, are really novel ways of looking at, you know, HFpEF and left-sided heart disease with novel mechanisms. So, there are patients who I think will benefit from them outside of the standard, you know, kind of pharmacologic therapies, but it has been a challenge.

Dr. Raza:
I would add to that, too, that I think we didn't necessarily focus on it here, we were focusing on HFpEF PH, but I think a lot of the CPCH patients that we see in practice are also our advanced heart failure patients who often have HFrEF, and usually I think by the time that they have significant remodeling of their pulmonary vasculature, they're more in the end-stage of their disease and so, we're probably thinking more about advanced therapies. As Tom mentioned, we can see dramatic improvements with LVAD therapy in those advanced-stage patients. But perhaps thinking about what we call sort of like the C2 patients, not really stage D but who are sort of transitioning. Do we think about, you know, is that high PVR another area that we can target by enrolling in clinical trials to sort of kick the can down the road of advanced therapies further? And then I think also maybe a way to think about it is when many of us have

patients in the revolving door of recurrent heart failure admissions, when we're thinking about offering things such as, you know, CardioMEMS are now enrolling in some of the more recent trials with the Cordella system and PROACTIVE, do we think about also, you know, we're going to have invasive hemo's on all of those patients, you know, we should be detecting CPC-PH thinking about enrolling in clinical trials in that space.

Dr. McLaughlin:
So, I've asked you two really hard questions, so I'm going to ask you a really easy and practical question. You know, when I see these patients in clinic, like the basics are just not being done, right? It's the little old lady that doesn't want to take her Lasix because she has to go to the bathroom too much, you know, and has never counseled about sodium, and blood pressure is out of control. Like, how do you really convey to both the patients and, you know, primary care doctors and general cardiologists, like, really how to manage just some of the baseline, like diuretics in specific? Like, if people – and I know that volume control is hard work and is not often reimbursable, but how do we get that message out to the community to the patients and the front-line doctors who see these patients?

Dr. Patel:
Well, I think it's challenging. I think, you know, a lot of patients, you know, with regard to the therapies, it's very important whenever I see patients who come to me that are typically elderly, they're typically on multiple medications, you know, and suffer from polypharmacy, and they're, you know, quite frankly sick and tired of taking an additional pill and an additional pill. And especially because at that age, a lot of these patients with elderly HFpEF, quality of life is extraordinarily important to all of us, but especially important to them. And a lot of times, you know, if you ask them, and I do ask them, you know, quality and quantity of life, you know, kind of where do you stand? It's, you know, I need to make the most of whatever time I have left. And if Lasix is preventing them from doing those things that they want to do, they're just not going to take it. But I try to impress upon them staying out of the hospital, timing of medications when you take it, so that one, you're not up all night, or two, you're not running to the bathroom when you're out and about, with the goal being keeping you out of the hospital, being with family, being able to do the things that you're doing. Because if you do get hospitalized that sets your quality life back much more than, you know, the quality of life hit that it takes when you take a daily medication that comes with some side effects.

I do think it often requires multiple touchpoints in a clinical setting. We have to see these patients frequently and often to impress upon them these points and it's challenging to do that in, you know, 15 to 20 minutes or less, you know, when you have that with a patient. And so, we typically see these patients very frequently when we're getting to know them, impress upon them some of these foundational aspects, weighing yourself daily same time of the day with the same amount of clothes on, salt discretion and dietary modifications, and rationale for why we're giving you these pills and why it's not just an additional pill, but because it could improve your quality of life long term. But if you don't have multiple touchpoints with either us, or a nurse practitioner or PA team, or nurse clinicians who communicate with them through the MyChart system, it can get lost and it's not possible in, you know, 10 to 15 minutes to do so.

Dr. Cascino:
Yes. I think education, education, education. And it just takes time. Education for each one of these diseases. You know, all these conditions come together and so, you know, helping to understand the patient's goals I think is first and foremost because that's what we're trying to achieve, and then setting expectations, and you know, how, you know, increasing physical activity and losing weight is going to help with these symptoms, and we'll makes sure your AFib is adequately treated. And so taking the time to help them understand why and really emphasize things that have evidence. You know, we have medications now helping them understand the rationale behind the medications. We spend a lot of time talking about sodium and fluid restriction, and the reality is we don't have a ton of evidence about it. It's part of our core package that we go through for all of our heart failure patients, but it's not something that's ever been shown to help people stay out of the hospital. And so that's honestly the thing I talk about the least. I'll talk about it if the patient brings it up and asks me about it, but otherwise we have no evidence to say that that helps. We do have evidence that SGLT2 inhibitors may help you stay out of the hospital, and so that's where I try to focus my time.

But it is a long-term thing. There's no easy fix for any of these things, and so I think keeping patients involved in our clinics and starting to enroll in clinical trials, which brings us back to the last question, I think is the next step because we are starting to have some trials that have shown some promise for the first time in the history of HFpEF.

Dr. Raza:
And then I'll just add to that, just in terms of, you know, thinking about polypharmacy, which is especially a problem for a lot of our, you know, elderly HFpEF patients, that there is the availability of a lot of poly pills. And so many of our HFpEF patients have hypertension and there's a wide variety of combinations of calcium channel blocker with thiazides, or thiazides with an ACE or ARB. Instead of adding another pill for them to take, we can the diuretic effect along with, you know, improved blood pressure control. So, something to keep I mind that I think has been more successful for certain of my elderly patients. And then also I find that a lot of the elderly patients really

like the CardioMEMS or now being enrolled in the Cordella. They like having their numbers everyday of like, what they're PA pressures are and what's their blood pressure and I have them come into clinic with an Excel spreadsheet of where all their pressures have been and I think it also helps the patient feel more empowered and a part of their care, and I find that that's been, you know, really successful.

Dr. Cuttica:
You just answered my question. I was going to ask in the older patient population that you describe with questionable time-to-benefit ratio of talking about salt and all of that, it is your sense, obviously as you said, Yasmin, or is there data to back up that doing something like CardioMEMS really does impact the care of these patients? So, you have a hard number for them to target rather than like, oh I got to count how much salt is in this?

Dr. Cascina:
There's data if you use the data. So, I mean, the CHAMPION trial showed a reduction in hospitalizations. I think the biggest limitation to them is you see them occasionally put in and then no one follows it, and so if no one follows it, it's not going to help. But for patients that are able to do it each day, and if you have the support. Because it takes time for someone to go in and look at the results and let the patient know what they should be on. You know, in currently available systems the patient can't see the number themselves, but if you have that infrastructure, it can work fantastic for the right patient.

Dr. Moles:
I'm going to ask a logistical question that I struggle with a little bit when seeing these patients that I think they have HFpEF, they may not. They have an intermediate echocardiogram, it's not completely HFpEF, it's not completely, you know, pre-capillary PH, and I've heard two train of thoughts on the timing of invasive hemodynamics. Do you do a right heart cath up front to prove that these patients have elevated left-sided filling pressures? Do you try to optimize them first and then cath them, but you may have a normal wedge pressure because you've done a great job and now you have a PVR of 3.1, 3.5 and they now have a diagnosis of PH? How do you go through that thinking process, if you don't mind?

Dr. Raza:
So, typically in my own practice, yeah, it's not a one-size-fits-all answer for sure, and it's definitely a tricky area, but I can say if I have a patient who really does not have any of those underlying PAH risk factors that I'd be worried about, you know, missing a significant pre-capillary disease even at an early presentation that's not overt on echo like scleroderma or, you know, a pulmonary hypertension patient, you know, methamphetamine use, HIV, and so on.

If it seems that they have, you know, sleep-disordered breathing, very comorbid with HFpEF and they are an intermediate probability based on the echo, like, you know, the H2FPEF score really comes out as intermediate, many of them will not have necessarily elevated natriuretic peptides we know because of the increased adipose tissue. Then if I'm really trying to understand their functional limitation, then I will send them for an exercise right heart cath to confirm that to make sure that I'm not just starting them on SGLT2 inhibitor and an MRA without any evidence that that's going to really help improve their symptoms or reduce hospitalizations. And actually I just had a patient where I think her H2FPEF was 3 to 4, she was obese. She was actually, before I met her, had recently been started on GLP-1 agonist. By the time we got a cath scheduled, she had already lost like, 50 pounds and her symptoms were completely resolved, and that's not something that we then ended up going on to cath. But that's how I sort of go through in my process.

Dr. Patel:
Yeah. If there are other indications for some of these therapies, like an SGLT2 based off of non-albuminuric or albuminuric CKD, type 2 diabetes, like, I wouldn't hesitate to start them if we can. So, maybe not for the indication of potentially HFpEF while undergoing a diagnostic evaluation, but for these other reasons because I think the risk of delaying that therapy for these other indications is outweighed by the potential benefit of starting them in a specialty. Like, for example as Dr. Raza mentioned, the GLP-1-receptor agonists, you know, there's marked reduction in CRP levels with the initiation of GLP-1 receptor agonists in the STEP-HFpEF trial. Whether that's all due to, you know, weight loss, we clearly see a reduction in systemic inflammation with this class of medications. And in the obese patient who is dyspneic, I think it should be considered as early as possible. That's a good situation to be in. I would argue that it's the optimal situation to be in. You've made the patient feel better, you haven't delayed their care in any way, and so if they are overtly congested in the office and we need to stave off a hospitalization, for sure I will start some therapies that, you know, may not be as evidence-based, the loop diuretics, but just to get them to a point where we can at least get them feeling a little bit better to be able to potentially be on the recumbent bike to see what their exercise physiology looks like.

Dr. Cascino:
Thank you.

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