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Albuminuria and Heart Failure: Connecting the Dots to Optimize Care

Announcer:
You're listening to *Conversations in CV Risk Assessment* on ReachMD. Here's your host, Dr. Jennifer Caudle.

Dr. Caudle:
This is ReachMD, and I'm your host, Dr. Jennifer Caudle. And joining me to discuss the relationship between albuminuria and heart failure is Dr. Robert Mentz. Not only is he an Associate Professor of Medicine in Population Health Sciences at Duke University in Durham, North Carolina, but he's also a member of the Duke Clinical Research Institute. Dr. Mentz, welcome to the program.

Dr. Mentz:
Thanks so much. I'm looking forward to the discussion today.

Dr. Caudle:
Absolutely. We're thrilled to have you. So to set the stage for our discussion, Dr. Mentz, can you tell us why albuminuria is gaining attention in heart failure management?

Dr. Mentz:
Absolutely. So this is an exciting new time where we have a new tool in our toolkit. Historically, many of our listeners may have not routinely checked uACR in patients with cardiovascular disease, or specifically those with heart failure, but now we know the increased prognostic utility of this marker and we have key therapies that not only treat heart failure but can help treat underlying kidney disease.

So this albuminuria, or albumin in the urine, reflects underlying vascular injury and endothelial dysfunction, both of which are really common in patients with heart failure and are central to the underlying pathophysiology. So a uACR provides important prognostic information above and beyond GFR. So we know when we get a BMP, we'll see that creatinine and can calculate a GFR, but we know that with a uACR, by checking the urine, we can get an additional marker of underlying kidney dysfunction. And this helps identify those patients at the highest risk for cardiovascular as well as kidney events, and helps us better treat our patients.

Dr. Caudle:
With that background in mind, let's dive into some data. In the pooled analysis of EMPEROR-Reduced and EMPEROR-Preserved, we saw that elevated urine albumin-to-creatinine ratio, or uACR for short, was associated with an increased risk of both first and recurrent heart failure hospitalizations as well as cardiovascular and all-cause mortality. From your perspective, what stands out about these findings? And how do they reinforce the clinical value of uACR in managing heart failure?

Dr. Mentz:
Yeah, thanks so much. So it's a really important question. And to remind our listeners, the EMPEROR program were trials in patients with heart failure, regardless of diabetes status, and it was two different trials: a reduced ejection fraction trial and a preserved ejection fraction trial looking at SGLT2 inhibitors with empagliflozin. And what we saw was that there were important cardiovascular benefits across the ejection fraction spectrum, and actually, it was the first large trial to demonstrate a clear positive benefit in patients with HFpEF, importantly.

And in addition to those cardiovascular benefits, we are now improving our understanding around the renal benefits as well. So we saw early data showing improvements in GFR. But now, with these exciting new data looking at uACR and incorporating the prognostic utility of this measure, when patients with heart failure have an elevated uACR above and beyond their underlying renal function, we know that they are at increased risk for both cardiac and kidney events. And importantly, these data were consistent across the ejection

fraction spectrum, really showing this as a unifying risk marker in heart failure.

So we now know that with uACR, which is a low-cost, easy test to incorporate into our clinical workflow, we need to think not only about getting blood work for our patients, but also urine studies, and specifically a uACR, so we can better understand their risk and think about longitudinal disease monitoring and management.

Dr. Caudle:
And building off of that, a review of recent data from the *Journal of the American College of Cardiology* found that albuminuria is associated with worse outcomes in heart failure across all ejection fraction categories, including heart failure with preserved ejection fraction, which is also known as HFpEF. Given that reliable biomarkers for HFpEF are still limited, how do you think uACR might fill some of the gaps in risk stratification or treatment planning for these patients?

Dr. Mentz:
Yeah, this is a really foundational question, and it's an exciting time for HFpEF, both in diagnosis and management, as historically, we didn't have a lot of therapeutic options; we were thinking about optimizing volume status. But now we have a number of trials demonstrating new therapeutic interventions that improve outcomes.

And how does uACR and kidney function fit into that? Well, we have an evolving understanding, and this really nice state-of-the-review, as you just noted, summarizing the role of checking uACR across the spectrum of heart failure, but really some novel insights in patients with HFpEF.

We know that we don't have a lot of other diagnostic markers for these patients. We check a natriuretic peptide level, but we know that in patients with HFpEF, particularly in the setting of obesity, that may be falsely low. A natriuretic peptide level may also be low, but they could have significant underlying symptoms related to congestion, particularly with exercise or activity level.

So to me, since we see this strong overlap between comorbidities and heart failure, especially in patients with HFpEF, we can now look at a uACR to have an additional underlying early marker to help risk-stratify our patients who may not otherwise have a lot of markers that we can incorporate into their evaluation and triage.

And since HFpEF is driven by systemic inflammation and microvascular dysfunction, albuminuria really reflects a key underlying pathophysiological abnormality that now can help tailor our care strategies around.

Dr. Caudle:
Excellent. For those of you who are just tuning in, you're listening to ReachMD. I'm your host, Dr. Jennifer Caudle, and I'm speaking with Dr. Robert Mentz about how albuminuria can inform heart failure care.

So Dr. Mentz, now that we've established the connection between albuminuria and heart failure, let's talk for a moment about how this relationship works. What does an elevated uACR tell us about a patient's physiology, particularly in terms of hemodynamic stress, fluid retention, and microvascular dysfunction?

Dr. Mentz:
So it’s really a great question. And what we know is that an elevated uACR reflects the increased glomerular pressure and capillary leak, which are signs of systemic hemodynamic stress and endothelial dysfunction, which are key drivers of heart failure, particularly in those patients with HFpEF. So we now have a key marker that helps us take a deeper dive into the systemic processes, particularly at the level of the kidney, around both endothelial and vascular dysfunction.

And I would underscore, as we just noted, this is above and beyond a GFR. So this gives us independent information from checking creatinine or blood work in our patients. And this uACR can indicate fluid overload and impaired sodium handling at the level of the kidney, which are key drivers of heart failure progression and kidney progression, and can signal broader microvascular damage across organ systems.

Dr. Caudle:
And thinking about applying this knowledge in practice, how do you see the cardiologist’s role shifting then when it comes to recognizing and managing elevated uACR? Is this something we—or rather, they—should be routinely checking?

Dr. Mentz:
Yeah. So I love this question because it took me some time to incorporate uACR into my practice, and now I'm really reaping the benefits of seeing the utility of this. So a quick answer is yes, we should be checking uACR in our patients with cardiovascular disease, as today we're really focusing on heart failure. This is an important measure that helps us risk stratify and think about therapeutic interventions for our patients.

So given the cardiovascular implications of albuminuria that are becoming more and more clear and evolving data about the benefits of medications like SGLT2 inhibitors on cardio-kidney effects, cardiologists and clinicians broadly need to be thinking more about a proactive role in screening for elevated uACR. We can't wait. We can't defer to a nephrologist, which might be weeks and months away for a patient to visit. So our clinicians across the cardiovascular spectrum and multidisciplinary teams need to be checking this. Routine uACR testing can be incorporated into heart failure management to help risk stratify, guide therapy adjustments, have these discussions with our patients about their underlying cardiovascular health, and collaborate more closely across their care team, including with our nephrology colleagues.

Dr. Caudle:
Thank you. And before we wrap up our program, Dr. Mentz, do you have any final thoughts that you'd like to share with our audience?

Dr. Mentz:
Yeah, I think some of it is just that we now have this measure with uACR that our nephrology colleagues have been using for a lot longer. But let's incorporate this into our cardiovascular practice. In order to use the data, you've got to check it. So incorporate this into your routine clinical workflow.

And then you can have these conversations with your patients as well, as an additional measure that they can look at. Patients with heart failure will often ask what their ejection fraction is, how's that kidney number looking? And they often know about the creatinine. But now we can incorporate uACR into our discussions with our patients.

Dr. Caudle:
That's excellent. And as a family doctor, I can say that we need to be on that bandwagon as well.

As those key insights bring us to the end of today's program, I'd like to thank my guest, Dr. Robert Mentz, for joining me to discuss albuminuria's impact on heart failure outcomes and how it can shape our management approaches. Dr. Mentz, it was great having you on the program today.

Dr. Mentz:
Thanks so much. I really enjoyed our conversation.

Announcer:
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