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Management of Elevated Albuminuria: Examining Therapeutic Pathways

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

Dr. Caudle:
Welcome to ReachMD. I'm your host, Dr. Jennifer Caudle, and joining me to share practical strategies for managing elevated albuminuria are Drs. Leslie Gewin and Robert Mentz. Dr. Gewin is a Physician Scientist in the Division of Nephrology at Washington University in St. Louis, Missouri, and a Staff Physician at the St. Louis VA. Dr. Gewin, thank you so much for being here today.

Dr. Gewin:
Thank you for having me. I'm excited to be participating.

Dr. Caudle:
Well, thank you. And Dr. Mentz is an Associate Professor of Medicine in Population Health Sciences at Duke University in Durham, North Carolina, as well as a member of the Duke Clinical Research Institute. Dr. Mentz, it's great to have you with us as well.

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

Dr. Caudle:
Thank you. So we're going to start with you, Dr. Gewin. Why is albuminuria so important in clinical decision-making? And what are the first steps we should take when a patient's urine albumin-to-creatinine ratio, or uACR for short, is elevated?

Dr. Gewin:
Thank you for that question. I think of the uACR as really a big red flag when I'm trying to risk stratify my patients. There's been a lot of data that shows that an increase in urinary albumin-creatinine ratio, or uACR, is associated with a more rapid decline in kidney function, increased cardiovascular events, and increased all-cause mortality. So this is definitely cause for concern when you notice that your patients have an increased uACR.

As a matter of fact, because of this strong association between increased uACR and adverse outcomes, it's been integrated in terms of how we risk stratify patients with chronic kidney disease. So now, because it's an additional concern besides just the estimated GFR looking at the kidney function, we also incorporate the uACR into our risk stratification. So patients who have uACR greater than 30 milligrams per gram would be considered elevated, between 30 and 300 moderately elevated, and above 300 severely elevated.

And so when we do see a patient who has elevated uACR, I think it's important to confirm. If it's severely elevated, I will rule out other causes of increased protein in the urine, and then I really take a look at their medications and try to understand how we can tweak their treatment to help reduce these increased cardiovascular and CKD progression risks associated with the increased uACR. And we're very fortunate that we have a lot more tools in our toolbox today than we did 10 years ago to help address this.

Dr. Caudle:
With that background in mind, Dr. Mentz, let's zero in on some specific therapeutic classes. Starting with SGLT2 inhibitors, who are great candidates? When should we initiate treatment?

Dr. Mentz:
Great. So thanks so much for that question. And building on that nice background, I think the framework of CKM, or cardio-kidney-

metabolic disease, is really helpful here as you think about those patients who might be good candidates for an SGLT2 inhibitor.

So starting with that M, the metabolic piece of this, for patients with diabetes, we know that there are not only the hemoglobin A1c benefits, but benefits around both cardio and kidney outcomes for those patients.

And moving toward that kidney population, we now have a multitude of studies, and I would highlight those with dapagliflozin and empagliflozin that have looked at patient populations with kidney disease, regardless of diabetes status, including elements such as uACR. And what we see is that there are important clinical outcome benefits in those with kidney disease, regardless of diabetes status, and it has benefits on both the heart and the kidneys.

And then finally, for that cardiovascular population, we know that those with a prior cardiovascular event as well as, importantly, those with heart failure, that there are key benefits on both the heart and the kidneys when we use SGLT2 inhibitors.

So I'd emphasize the utility of SGLT2 inhibitors across the spectrum of cardiovascular, kidney, and metabolic disease. We can incorporate uACR for both benefits around the heart and the kidneys. And we need to start these drugs promptly.

One of the things is that, when we have a busy clinic visit and we're talking to our patients about new therapeutic options, it can become this clinical inertia where we say we will consider talking about SGLT2 inhibitors at the next visit. I'd really urge the listeners to incorporate SGLT2 inhibitors routinely in clinical practice across the cardio-kidney-metabolic spectrum.

Dr. Caudle:
Those are great points. And staying with you for another moment, Dr. Mentz, what role do ACE inhibitors and ARBs play in managing albuminuria? And what does the decision-making process look like for those?

Dr. Mentz:
Really great questions. So we know, building upon the exciting more recent data, with SGLT2 inhibitors—and we'll talk about GLP-1 receptor agonists here shortly—we know we have these foundational therapies in ACE inhibitors and ARBs. These are recommended in patients with hypertension, diabetes, and chronic kidney disease. So it's similarly a multitude of different disease states.

And albuminuria is a key consideration as we think of their underlying kidney risk. We need to institute ACE inhibitors or ARBs promptly, and we need to titrate to the maximally tolerated dose.

We know that there are both cardiovascular and kidney benefits as we increase to the maximally tolerated dose, or that dose where blood pressure is still tolerated and we can carefully monitor kidney function and electrolytes, including potassium. But ACE inhibitors and ARBs, really in sum, are a foundational therapy in those with chronic kidney disease.

Dr. Caudle:
Thank you. And for those of you who are just tuning in, you are listening to ReachMD. I'm your host, Dr. Jennifer Caudle, and I'm speaking with Dr. Leslie Gewin and Dr. Robert Mentz about therapeutic pathways for elevated albuminuria.

Now, Dr. Gewin, having talked about SGLT2 inhibitors, ACE inhibitors, and ARBs, there's one more class I'd like to touch on, and that's GLP-1 receptor agonists. Who qualifies for this treatment? And when is it the optimal approach?

Dr. Gewin:
Thank you very much for that question. I think there's really exciting data with the use of these GLP-1 receptor agonists and chronic kidney disease.

First of all, there was the FLOW trial in the *New England Journal of Medicine*, which said that patients that have CKD, diabetes, and elevated albuminuria had a reduced incidence of cardiovascular mortality and all-cause mortality with the use of GLP-1 receptor agonists.

So this is very exciting, because a lot of our patients who have chronic kidney disease are at really increased risk for cardiovascular events. So a drug that can actually improve cardiovascular mortality has the potential to have a huge impact. This class of drugs has also been shown to have protective effects in terms of CKD progression in patients who have obesity and established cardiovascular disease.

There's still some questions, I think, about the exact mechanism of action, and there's some ongoing studies which should answer those questions. But I think that this class of drugs is really helpful for patients who have chronic kidney disease, an elevated uACR, and who are at high risk for cardiovascular events, including those with obesity.

Dr. Caudle:
Excellent. And before we wrap up our program, I'd like to zoom out and ask each of you a big picture question. And starting with you,

Dr. Mentz, how do lifestyle modification strategies fit into these treatment pathways?

Dr. Mentz:
That's really an important question, and something that our patients are very interested in. So importantly, we not only have excellent pharmacotherapies now, as we think of ACE inhibitors, ARBs, SGLT2 inhibitors, GLP-1 receptor agonists, and also mineralocorticoid receptor antagonists in some populations.

But we need to focus on the total picture, and they're those lifestyle changes—diet, nutrition, and exercise—that we know help our patients. We can focus on weight loss, healthy living, and lifestyle, and these medications may have increased benefit when we have holistic management for our patients and are working to optimize their weight, their glycemic control, and their blood pressure. And all of these things in concert are what will give us the best opportunity to help the quality of life and clinical outcomes for our patients across the cardio-kidney-metabolic spectrum.

Dr. Caudle:
Excellent. And Dr. Gewin, I'll turn to you for the final word. At what point should we refer to a nephrologist? And how can we optimize system level support to ensure timely action?

Dr. Gewin:
Yeah, this is really important. You know, the guidelines suggest that a patient should be referred to a nephrologist when their estimated GFR falls below 30 and/or they have an elevated urinary albumin-creatinine ratio greater than 300. And while this is important, I think it's also necessary to consider that there is a shortage of nephrologists and a growing demand for care for the CKD population, therefore, a lot of the care is going to need to start with primary care physicians.

By the time a patient's eGFR has dropped below 30, it's pretty advanced, and some of these medications and strategies that we've talked about in terms of reducing the uACR really should be started much earlier.

Therefore, I think it's going to be really important to pursue novel ways to integrate with the medical chart alerts or ways for our very busy primary care physicians to integrate some of these therapies into the care of their patients.

Dr. Caudle:
That's a great comment for us to think on as we come to the end of today's program. I'd like to thank my guests, Drs. Leslie Gewin and Robert Mentz, for joining me to discuss how we can manage elevated albuminuria. Dr. Gewin and Dr. Mentz, it was great having you both on the program today.

Dr. Gewin:
Thank you so much for the invitation. It was an honor to participate.

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

Announcer:
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