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Albuminuria: An Overlooked Red Flag in Cardiovascular Risk

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

Dr. Sorrentino:
Welcome to ReachMD. I'm Dr. Matthew Sorrentino, and joining me to discuss the critical role of albuminuria in cardiovascular risk prevention is Dr. Ashish Verma. Dr. Verma is an Assistant Professor of Medicine in the Section of Nephrology at Boston University, Chobanian and Avedisian School of Medicine. He's also a physician at Boston Medical Center and the lead nephrologist for the Boston University Amyloidosis Center. Dr. Verma, it's great to have you here today.

Dr. Verma:
Yeah, nice to be here.

Dr. Sorrentino:
To set the stage for our discussion, Dr. Verma, can you walk us through how our clinical understanding of albuminuria has really evolved even beyond kidney disease recently?

Dr. Verma:
Yeah, sure. This is an excellent question. So albuminuria is traditionally viewed only as a marker of kidney disease. We use albuminuria to diagnose chronic kidney disease and also to risk stratify chronic kidney disease. But over the years, we are now learning that albuminuria is a marker of systemic vascular injury and also an important cardiovascular risk marker. To quote some of the studies, even low levels of albuminuria within normal or mildly increased levels is associated with incident heart failure, myocardial infarction, and cardiovascular death.

It shows you how strong this biomarker is. And recently, AHA incorporated this biomarker for cardiovascular-kidney-metabolic syndrome staging. It's a modifiable biomarker. You can lower albuminuria using antiproteinuric therapy like ACE inhibitors, ARBs, SGLT2 inhibitors, and non-steroidal MRA antagonists.

So I would say the major thing that we have learned is that albuminuria is an early red flag for cardiovascular risk.

Dr. Sorrentino:
That's great. As a cardiologist, I really didn't think of how much the kidney markers added to cardiovascular risk prevention. But we can look at some of the more recent data that shows really how robust this marker can be.

A recent review from the *Journal of the American Medical Association* entitled *Estimated Glomerular Filtration Rate, Albuminuria, and Adverse Outcomes* examined this impact of albuminuria, not just on kidney function, but on cardiovascular and other health concerns. This was in over nine million individuals from 1980 to 2021. And it found that a higher urine albumin-to-creatinine ratio, or uACR, was associated with a more stepwise increase in risk for a number of adverse outcomes that they studied, which included acute kidney injury, but also myocardial infarction, stroke, cardiovascular mortality, and all hospitalizations.

So given this breadth of a stepwise risk, what do these results signal to you about how we should interpret even just mild increases in uACR?

Dr. Verma:
Yeah, so this study is very important, using the CKD Prognosis Consortium of over nine million individuals showing a dose-response relationship between albuminuria, cardiovascular outcomes, and kidney outcomes as well. So the biggest message from this study is

that there is no safe threshold for albuminuria.

Even from my own work, we have learned that even albuminuria around seven milligrams per gram is associated with future cardiovascular death, myocardial infarction, and heart failure. So it shows you that even mild elevation of albuminuria is clinically significant. It's reflecting systemic vascular health, not just kidney disease.

So I think the clinical implication here is not to take this albuminuria as benign when it is very low level. It gives you an opportunity for prevention, and also to identify individuals who are higher risk for progression of albuminuria and higher rates for cardiovascular risk in the future.

Dr. Sorrentino:
There was another study recently published in *Heart*. It looked at data from over 450,000 patients. It was entitled *Prognostic Impact of Albuminuria in Early-Stage Chronic Kidney Disease on Cardiovascular Outcomes*. The study found that in early chronic kidney disease—as you're saying, some of these markers at very early stages—albuminuria was independently associated with increased risk of major adverse cardiovascular events like heart failure and all-cause mortality.

In light of these findings, what stands out to you about the predictive power of albuminuria in these very early kidney disease patients? I'm thinking about patients that have CKD 1 and 2, and may have just a little bit of albumin. How should we think about those patients?

Dr. Verma:
Yeah, so this is a very interesting study giving an important message—especially to primary care physicians and even cardiologists—to not just fixate on eGFR. So this study's showing you that albuminuria actually adds prognostic value even with preserved GFR.

Then we are thinking, okay, this patient has an eGFR of 70. Oh, it's okay, this patient doesn't have CKD. But if this patient is having 300 miligrams per gram of albuminuria, this patient is actually at a very high risk for cardiovascular events in the future. So risk is not only about kidney function, but also systemic vascular injury and microvascular dysfunction.

So I think the clinical implication of this study is to measure uACR in early CKD as your tool, and also use it with eGFR for risk stratification.

Dr. Sorrentino:
For those just tuning in, you're listening to ReachMD. I'm Dr. Matthew Sorrentino, and I'm speaking with Dr. Ashish Verma about the importance of monitoring albuminuria in mitigating cardiovascular risk.

So in thinking about this research that we've been discussing, Dr. Verma, I'd like to talk about some real-world applications of this data. Despite the findings that position albuminuria as a key cardiovascular risk factor, I find that urine albumin-creatinine ratio is underused. I don't really, or haven't until recently, ordered it very much in many of my prevention patients. Why do you think that is the case? And how do we really inform cardiologists and primary care providers that this is an important risk marker?

Dr. Verma:
Yeah, so this is a real gap in implementation. Historically, albuminuria is seen as a kidney test, so most of the primary care physicians or cardiologists use it to diagnose chronic kidney disease, not for cardiovascular risk assessment. And testing practices actually vary across clinics. There is no standardization of how to check albuminuria.

And it's also not integrated into CV risk assessment. Recently, AHA came up with PREVENT score, which uses uACR and eGFR now.

So I think the awareness about uACR as an important cardiovascular risk factor is still evolving. It's a missed opportunity. It's an inexpensive test and gives you powerful insight into cardiovascular risk and kidney risk. So I think there is a huge opportunity to check albuminuria in patients like with hypertension, heart failure, atherosclerotic cardiovascular disease, and chronic kidney disease.

Dr. Sorrentino:
I'm glad you brought up the PREVENT score. I was going to ask you about how that may change our use of this marker. As you pointed out, the PREVENT score is now in the new hypertension guidelines. It adds uACR and eGFR into our equation.

So do you think this will help address some of these gaps? And in terms of how to use this, should these tests be more embedded into our electronic medical record? Are there ways that we can have this test really at the forefront of our way of assessing patients?

Dr. Verma:
Yeah. So I think there is two-way approach. One is what we can do in clinics. So as you told, there is more awareness about albuminuria as a respect of cardiovascular risk. And thankfully, the PREVENT score will help in that people, mostly the physician, will check albuminuria in high-risk patients with hypertension or cardiovascular disease.

So I would say in clinics, I think we should make uACR routine testing, annual testing, in people with diabetes, hypertension, CKD, and atherosclerotic cardiovascular disease. We should standardize testing. We should tell clinicians, you need to use uACR as a test. Spot uACR can be used to check albuminuria. And then we have the result, and we have patients with high albuminuria. We should be guiding therapy. We should be putting them on ACE inhibitors, RAS blockers, SGLT2s, or non-steroidal MRA antagonists.

And we should also communicate to patients using uACR if they have cardiovascular risk, and we should tell them that it's an early red flag.

And in a system-level approach, I think there is emergence of large language models now, artificial intelligence. We should embed uACR or eGFR into our Epic. We should give red flags whenever patients are having moderately increased albuminuria. And I think this should help to prevent cardiovascular event in the future. This should help in implementation of antiproteinuric therapy. We have so many drugs now for heart failure and chronic kidney disease.

Dr. Sorrentino:
That sounds great. In our last few minutes, Dr. Verma, any final takeaways on using these markers? Should we be measuring them annually, every six months, just in certain patients, in all of our patients?

Dr. Verma:
Yeah. So to start, I would say that albuminuria is a powerful early warning sign of cardiovascular risk; even mild elevation predicts adverse outcomes.

There are multiple guidelines for screening albuminuria, like annual testing in patients with diabetes, hypertension, chronic kidney disease. I would say people should be checking albuminuria regularly to see the response to antiproteinuric neurotic therapy. Because you want to make sure, if you are putting patient on an SGLT2 inhibitor or a combination of therapy of SGLT2 and non-steroidal MRA antagonists, you should see a reduction in albuminuria.

If there is no reduction, there is a residual risk. And now we have combination therapies. This test is inexpensive, widely available, actionable, and should be treated like blood pressure and LDL. It's a very important marker. So I think embedding uACR into routine practice can save lives and prevent future cardiovascular events.

Dr. Sorrentino:
I think those are great comments, and as I move to my clinic later today, I will probably be ordering more of this to see what type of risk our patients have.

I want to thank my guest, Dr. Ashish Verma, for joining me to discuss how albuminuria is reshaping our understanding of heart and kidney health. Dr. Verma it was great having you on the program today.

Dr. Verma:
Thank you so much for having me.

Announcer:
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