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UACR in Diabetes: A Window Into Cardiorenal Risk

Announcer:
This is *Diabetes Discourse* on ReachMD. Now, here's your host, Dr. Brian McDonough.

Dr. McDonough:
You're listening to *Diabetes Discourse* on ReachMD, and I'm Dr. Brian McDonough. Joining me to discuss the link between elevated UACR and cardiovascular risk in patients with diabetes is Dr. Jennifer Green. She's a Professor of Medicine at Duke University School of Medicine in Durham, as well as a faculty member of the Duke Clinical Research Institute. Dr. Green, welcome to the program.

Dr. Green:
Hi, it's great to be here.

Dr. McDonough:
Let's start with the basics, Dr. Green. Why is UACR testing so important in people with diabetes, and how well is it being done in practice today?

Dr. Green:
The way that we identify whether or not people with diabetes or without diabetes have kidney disease is by looking at both their eGFR and their urine albumin-to-creatinine ratio, which is often abbreviated as UACR.

And those tell us different things about kidney function. If the eGFR is consistently less than 60 or if the UACR is consistently 30 milligrams per gram or higher, and those abnormalities are present for as short a period as three months, that's a person who, by definition, has chronic kidney disease. And you don't need to have both labs be abnormal.

We really have to do both tests so that we understand who has kidney disease and is at risk for either worsening kidney disease or the other kinds of problems that can be associated with that.

Dr. McDonough:
We know that UACR often goes hand in hand with EGFR. So how should clinicians interpret those two results together, and why do we need both?

Dr. Green:
That's the million-dollar question. So I have worked over the years with a lot of nephrologists, and this is something that I had to learn. Everybody's kidney disease is a little different, and some people with kidney disease have only a low eGFR, or only a high urine albumin-to-creatinine ratio. So they don't necessarily go hand in hand, although they often do. What we tend to see is, when people develop kidney disease and it progresses over time, the eGFR—estimated glomerular filtration rate—drops over time. But the UACR may become greater and greater over time as well.

But you don't really necessarily have to have both. Some people, again, will only have an abnormality in one of those tests. And we can be fooled if we only do the eGFR. And that's what happens a lot of the time—we're just looking at the eGFR that gets reported on standard blood chemistry tests. And if it remains over 60, we often aren't alert to the fact that our patient actually has evidence of kidney damage. We have to look at the UACR too, because it can often be abnormal when the eGFR still looks fine. So we need to know about kidney disease as early as possible and do both.

Dr. McDonough:
Now, if a patient presents with persistent albuminuria but a preserved eGFR, what does that signal about kidney and cardiovascular

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risk?

Dr. Green:
If you have a urine albumin-to-creatinine ratio that is above normal, and it's persistently above normal, that tells me a lot of things about your kidney health and what the future may hold for you, even if the eGFR is normal—if it's above 60.

So what that tells me is that there has been damage to the kidneys, so that albumin is leaking from the bloodstream out into the urine, and that's a problem that's indicative of kidney damage and is a risk for progressive kidney damage over time.

But interestingly, if you have albumin in your urine, it also is a key insight into your greater vascular health. And if you have an elevated UACR, that probably indicates that you have endothelial dysfunction and vascular damage that extends far beyond just the kidneys. And so people with an elevated UACR are not just at risk for worsening kidney function over time. It also means that they have an increased risk for cardiovascular events.

Dr. McDonough:
We also know that UACR can vary from one test to the next. So how should clinicians think about transient elevations, and what steps should we take before concluding that albuminuria is persistent?

Dr. Green:
That is important, and we don't want to diagnose patients with problems that they don't actually have. So that is one reason why we don't diagnose someone as having chronic kidney disease based upon one laboratory abnormality or laboratory abnormalities that are present only on one day.

So, if a patient has an elevated urine albumin-to-creatinine ratio, what I would do is, three months later, at their next appointment, I would repeat it. And I would probably also get a regular old urinalysis. I would want to make sure that it was a clean catch specimen, that it didn't have a lot of contaminants in it, and that there wasn't evidence, for example, of a urinary tract infection that might elevate the UACR test but not really be indicative of intrinsic chronic kidney disease. So we do want to check it again and make sure there's nothing going on that might cause a spuriously elevated value.

But otherwise, it's pretty straightforward. If a person's UACR is elevated on multiple different occasions, it's probably a pretty good indicator that they have chronic kidney disease and that we need to react accordingly.

Dr. McDonough:
For those just joining us, you're listening to *Diabetes Discourse* on ReachMD. I'm Dr. Brian McDonough, and I'm speaking with Dr. Jennifer Green about the cardiorenal significance of UACR in patients with diabetes.

So, Dr. Green, once persistent albuminuria is confirmed, how should clinicians use UACR changes over time to reassess cardiovascular and kidney risk?

Dr. Green:
So once the albuminuria is clearly persistent, there are a couple of different things that we need to do. First of all, we need to understand that that person has evidence of chronic kidney disease, for example, even if their eGFR is still in the normal range. And we want to understand, of course, as best as possible, why they might have kidney disease.

And in my clinic, many patients have kidney disease related to long-standing diabetes or poorly controlled hypertension. Those are some of the most common reasons in the United States. But we do need to make sure that we remain alert to the possibility that there could be other things contributing to kidney disease.

So again, that's where the plain old urinalysis comes in handy. If there, for example, are a lot of red cells in the urine, that's probably somebody who I'd refer directly to nephrology for input. But if I'm fairly certain that their kidney disease is related to the kinds of things that I manage in my endocrinology clinic, I feel personally responsible for addressing it. There are certain individuals who may need to see a nephrologist as soon as possible, though.

And, if you look, for example, at the KDIGO guidelines, they have a heat map that helps us plot out our own patient's eGFR and UACR and really figure out what stage of kidney disease and what stage of albuminuria they're currently in. For example, KDIGO recommends that for patients with severe albuminuria, they might need to see a nephrologist right off the bat.

But again, for the remainder of people—the majority of people—I'm going to introduce indicated and guideline-directed medical therapies to help mitigate the risks associated with chronic kidney disease. So, for example, in my clinic, I manage many patients with type two diabetes and chronic kidney disease. I make sure that they're on the maximum tolerated dose of ACE or ARB wherever

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possible. I make sure that they're on an SGLT2 inhibitor. If they have persistent albuminuria beyond that or have other indications for treatment, I will also incorporate the use of medications like a non-steroidal mineralocorticoid receptor antagonist like finerenone or a GLP-1 receptor agonist-based therapy.

And we do need to follow both the eGFR and the UACR over time, because if I've introduced those therapies that are supposed to slow the progression of kidney disease, but the UACR continues to worsen and it does not improve, that will really get my attention. I want to see the UACR go down when I introduce those treatments.

Dr. McDonough:
Well, as a follow-up to that, which patient factors, including persistent or rising UACR and changes in eGFR, should prompt clinicians to reassess cardiovascular and kidney risk and consider treatment adjustments?

Dr. Green:
If I'm introducing those therapies and the UACR just continues to rise, I would send that patient to see a nephrologist. Current guidelines for the management of chronic kidney disease in patients with diabetes recommend that we target, with our therapies, a reduction in UACR of 30 percent or greater. So that's really what I'm looking for. And sometimes it may take the addition of more than one treatment in order to achieve that.

Now, the tendency can be that, over time, chronic kidney disease and albuminuria will worsen, and that can also often be a clue that we need to intensify therapy or introduce and add additional therapies to address that persistently elevated or rising UACR value.

Now, remember, though, that many of these treatments that we use to preserve kidney function, when they are started or the dose increases, can often result in an acute drop in eGFR. And good examples of medicines that can do that are the ACEs and ARBs, our SGLT2 inhibitors, and, finerenone. So these are all interventions that have, in fact, generally favorable hemodynamic effects, both systemically and in the kidney. And so it is not unexpected to see a drop in eGFR when these therapies are introduced. However, I have again learned from nephrologists that as long as that dip in eGFR with the introduction of a new therapy is not greater than 30 percent, then it should not represent an acute kidney injury and, in fact, again, is reflecting a favorable hemodynamic effect. But that is something that takes some getting used to, and we don't like to see eGFR drop. Traditionally, we've considered that to be a bad sign. We need instead to understand that's an expected effect of the introduction of many beneficial therapies in patients with chronic kidney disease.

Dr. McDonough:
Finally, looking back on our conversation today, what's the main message you want clinicians to walk away with about UACR and cardiorenal risk in diabetes?

Dr. Green:
I think the main messages that I would like people to remember from this discussion would be to remember to screen for chronic kidney disease and diabetes with both the eGFR and the UACR. In the United States, we really probably only check UACR once a year in people with diabetes, somewhere between 10 and 40 percent of the time, depending on your location of practice. So we need to do much better than that to understand and appreciate our patients' risk, but also to understand that, really, we in endocrinology and primary care have many, many tools available now to address the risks associated with chronic kidney disease very successfully. So I would hope that people would feel empowered to act upon the abnormal results of tests that they might order. It doesn't mean the patient needs to go see nephrology. It doesn't mean that there's nothing that we can do. It really, in fact, is a clue and a sign to intervene early.

Dr. McDonough:
That's a very thoughtful reminder for all of us. And with that, I want to thank my guest, Dr. Jennifer Green, for sharing her insights on UACR as an indicator of cardiovascular and kidney risk in diabetes. Dr. Green, we really appreciate you joining us today.

Dr. Green:
Thank you for having me. I have also enjoyed the conversation.

Announcer:
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