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How Do the Drivers of Chronic Kidney Disease in Type 2 Diabetes Play a Role in Patient Care?

Announcer:
Welcome to Spotlight on Chronic Kidney Disease in Type 2 Diabetes on ReachMD. This medical industry feature, titled “How Do the Drivers of Chronic Kidney Disease in Type 2 Diabetes Play a Role in Patient Care?” is sponsored by Bayer and is intended for physicians.

Here’s your host, Dr. Edgar Lerma.

Dr. Lerma:
Hello, and welcome to part 3 of this 3-part video series focused on the unmet needs of patients with CKD and type 2 diabetes. My name is Dr. Edgar Lerma, and today, I will be talking with Dr. Eugene Wright, Consulting Associate in the Department of Community and Family Medicine in the Department of Medicine of Duke University Medical Center, and Dr. Javier Morales, Associate Professor of Medicine at the Donald and Barbara Zucker School of Medicine at Hofstra/Northwell on Long Island. We’ll be discussing the need for early screening for and diagnosis of CKD in patients with type 2 diabetes. Thank you both for joining us here today.

Dr. Wright:
Thank you for having me.

Dr. Morales:
Yes, thanks. Thanks for your invitation.

Dr. Lerma:
Before we begin, I just wanted to review some of the key points from the previous videos regarding the drivers of CKD in type 2 diabetes and the role of mineralocorticoid receptor or MR overactivation. CKD progression is dependent on the combined effects of metabolic, hemodynamic, and inflammatory and fibrotic factors. Inflammation and fibrosis is largely driven by overactivation of the MR. Under normal circumstances, MR signaling regulates electrolyte and fluid balance within the kidneys. However, under certain conditions like type 2 diabetes, the MR within the kidney can become pathologically overactivated. This leads to the production of proinflammatory cytokines and profibrotic proteins which can lead to injury and structural changes in the kidneys and the heart, in turn leading to declining kidney function, cardiovascular decline and ultimately end stage kidney disease. Dr. Wright, how prevalent is CKD?

Dr. Wright:
Thanks, Dr. Lerma. CKD is highly prevalent, affecting 15 percent of US adults, or approximately 37 million people. Despite this, awareness of CKD remains low.

Dr. Lerma:
Dr. Morales, why do you think that is?

Dr. Morales:
According to a 2014 study, more than 40 percent of cases of CKD stages 3 through 5 were undiagnosed, with the rate of diagnosis even lower among patients in the earlier stages of CKD. This is in part because CKD is usually silent until its late stages, with symptoms typically due to complications of reduced kidney function. Therefore, identification of CKD in patients with type 2 diabetes, especially in earlier stages, relies on assessment of kidney damage and kidney function, usually through laboratory tests for detection.

Dr. Wright:

I'll also add that the first step towards slowing down the progression of CKD and preventing harmful organ damage is early detection. Earlier detection allows more time for evaluation and treatment but requires explicit testing strategies for asymptomatic individuals with risk factors for CKD, such as type 2 diabetes.

Dr. Lerma:
Let's talk about the main tests used to determine how well the kidneys are functioning. The 2 main tests measure estimated glomerular filtration rate, or eGFR, and urine albumin-to-creatinine ratio, or UACR. Dr. Morales, can you give us a better sense of these tests respectively?

Dr. Morales:
Sure. eGFR measures how much creatinine, a waste product from kidney filtration, is in the blood. When eGFR levels decline, it is an indication that kidney function is worsening, making it a reliable indicator of later stage kidney damage. It is important to note here that certain medications used for managing blood pressure, as well as diuretics, will alter the eGFR. This is another factor that can often delay the appropriate diagnosis of CKD. Urine albumin/creatinine ratio, or UACR, in contrast, measures how much albumin, a protein usually found in the blood, versus how much creatinine, is in the urine. If increased levels of albumin are in the urine, this is an indication of kidney damage. The urine albumin/creatinine ratio is a more sensitive measure of kidney damage, especially earlier stage kidney damage.

Dr. Lerma:
Dr. Wright, turning to you, how are these tests used in the diagnosis of CKD?

Dr. Wright:
The eGFR and the UACR are used to define CKD in type 2 diabetes in the guidelines published by the National Kidney Foundation's Kidney Disease Outcome Quality Initiative, or the KDOQI; the Kidney Disease Improving Global Outcomes, the KDIGO; and the American Diabetes Association, the ADA. These guidelines define CKD as a clinical diagnosis based on the presence of albuminuria which is greater than or equal to 30 mg/g of creatinine and/or reduced eGFR less than 60 mL/min/1.73 m^2 in the absence of signs or symptoms of other primary causes of kidney damage in a patient with diabetes. For UACR, 2 of 3 specimens collected within a 3- to 6-month period of time should be abnormal before considering a patient to have high or very high albuminuria. For the eGFR, measurements must be less than 60 mL/min/1.73 m^2 for 3 months to diagnose CKD.

Dr. Lerma:
And we also know that both UACR and eGFR have been shown to be independent predictors of renal outcomes and progression of kidney disease. But coming back to the guidelines that Dr. Wright just mentioned, Dr. Morales, can you share what they recommend in terms of screening?

Dr. Morales:
Absolutely. The ADA recommends assessment of urine albumin/creatinine ratio and eGFR in patients with type 2 diabetes at least once a year. Unfortunately, the urine albumin/creatinine ratio screening rates are suboptimal among patients with type 2 diabetes. Among Medicare patients diagnosed with diabetes in the United States, there is less than 50 percent guideline adherence, with lower rates seen in older age groups.

Dr. Lerma:
Dr. Wright, why do you think that these rates are so low?

Dr. Wright:
There may be some logistical issues with albuminuria screening, including urine collection instructions, requirement for specific urine cups, or an inadequate patient recall system when patients don't bring a urine sample. Additional care from a diabetes support facility has been shown to be an important determinant of ACR measurement. The eGFR assessments, in contrast, have somewhat better adherence, but eGFR alone often misses early stages of CKD. Moreover, patients with high albuminuria of greater than 30 mg/g of creatinine are 1.5 times more likely than patients with normal levels of albumin to die from cardiovascular events, including myocardial infarction, heart failure, sudden cardiac death, or stroke, and this risk was found to be independent of the eGFR.

Dr. Lerma:
Dr. Morales, any thoughts to add here?

Dr. Morales:
Clinical and laboratory guidelines recommend urine albumin/creatinine ratio as the preferred measure of albuminuria. Urine albumin/creatinine ratio is best measured by a spot sample in the first morning void. While a timed albumin/creatinine ratio collection

can be done, this can be burdensome and add little to prediction or accuracy. The urine dipstick tests for UACR are not sufficiently sensitive, quantitative or standardized across manufacturers. One study found that over half of patients within the urine albumin/creatinine-based moderately increased risk and high-risk categories were classified into lowest categories when based on dipstick results.

Dr. Lerma:
And, unfortunately, related to the issues you both articulated, we do see in practice that patients with CKD and type 2 diabetes are most commonly referred to a nephrologist at stage 3 CKD or later. In a cross-sectional sample of US patients in 2008 that examined the onset of chronic kidney failure, only 57% received any nephrology care, while only 25% of patients were treated by a nephrologist for more than 1 year.

Dr. Morales:
In order to address the issue of early detection, explicit testing strategies are needed for asymptomatic individuals, especially those with high-risk factors for CKD like type 2 diabetes. The National Kidney Foundation has developed a new Healthcare Effectiveness Data and Information Set measure, or HEDIS measure, to improve kidney testing in patients with diabetes. The HEDIS measure will evaluate claims data to assess the percentage of adults with diabetes who receive both eGFR and urine albumin/creatinine tests during a 12-month period. This measure will hopefully improve rates of comprehensive kidney health evaluation in patients with diabetes to more consistently identify and treat CKD in this high-risk population.

Dr. Lerma:
Thank you, Dr. Morales. So we've established that early screening and diagnosis for patients with CKD and type 2 diabetes through both UACR and eGFR measurements is important. Practitioners who rely on eGFR alone will miss many patients' progression to CKD. But what are the best practices recommended once a patient is diagnosed? Dr. Wright, let's start with you.

Dr. Wright:
The National Kidney Foundation guidelines recommend managing CKD and type 2 diabetes through a combination of lifestyle modifications and pharmaceutical interventions. Lifestyle modifications are a part of a multifactorial risk reduction strategy that can include smoking cessation, a healthy diet, and exercise and weight loss among those who are overweight or have obesity. Pharmacological targets mainly include metabolic factors like elevated blood glucose and hemodynamic effects like elevated blood pressure or high intraglomerular pressure. However, inflammation and fibrosis are largely unaddressed.

Dr. Lerma:
Thanks, Dr. Wright. Dr. Morales, what are your thoughts?

Dr. Morales:
The KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease recommends that in people with CKD and diabetes, glycemic control should be part of a multifactorial intervention strategy addressing blood pressure control and cardiovascular risk. The ADA and the European Society of Cardiology also recommend optimization of glycemic control and blood pressure control to slow decline in kidney function, but we both know that even when blood pressure and blood glucose are controlled, patients still progress. In patients with diabetes, hypertension, and albuminuria, treatment with an ACE inhibitor or ARB is recommended. Despite these recommended treatments, even when optimized, patients with CKD and type 2 diabetes remain at high risk of developing end-stage kidney disease and cardiovascular complications.

Dr. Wright:
Just to add to what Dr. Morales said, advancements in glucose and blood pressure control have made important gains in reducing type 2 diabetes complications. This is especially true with regard to cardiovascular events. Despite these improvements, however, patients with CKD and type 2 diabetes still face a substantial risk of CKD progression. It is very important for patients and healthcare professionals to recognize that even with well-controlled blood glucose, or A1c, and blood pressure, many patients still experience CKD progression.

Dr. Morales:
And, as Dr. Lerma had mentioned before, CKD progression is dependent on the combined effects of metabolic, hemodynamic, and inflammatory and fibrotic factors. However, in the current treatment landscape, inflammatory and fibrotic factors are largely unaddressed. Inflammation and fibrosis of the kidneys can lead to declining kidney function, cardiovascular decline and ultimately end-stage kidney disease.

Dr. Lerma:
Before we close our discussion today, are there any additional takeaways you want to leave our listeners with for managing the drivers

of CKD and type 2 diabetes? Dr. Morales, I'll start with you.

Dr. Morales:
Thanks, Dr. Lerma. CKD and type 2 diabetes is currently managed by lifestyle modifications and by pharmacologically targeting risk factors such as hemodynamic and metabolic factors. Even with A1c and blood pressure control, there remains a risk for CKD progression.

Dr. Lerma:
Thank you, Dr. Morales, and Dr. Wright, you get the final word.

Dr. Wright:
Well, because early stage chronic kidney disease is usually asymptomatic, explicit laboratory tests are required for early detection. Early detection facilitates the appropriate diagnosis and treatment of chronic kidney disease, so it is very important for all patients with type 2 diabetes to be screened at least once a year with both the UACR and the eGFR.

Dr. Lerma:
Thank you both for your time today, and thanks to our listeners for joining us for the final episode of this 3-part series. If you have not already, be sure to check out the previous episodes focused on understanding the drivers and the cardiorenal connection of CKD in type 2 diabetes.

Announcer:
This program was sponsored by Bayer. If you missed any part of this discussion or to find others in this series, visit reachmd.com/chronickidneydisease. This is ReachMD. Be part of the knowledge.