Transcript Details
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What Cardiovascular Effects Are Associated With Chronic Kidney Disease in Type 2 Diabetes?

Announcer:
Welcome to Spotlight on Chronic Kidney Disease in Type 2 Diabetes on ReachMD. This medical industry feature, titled “What Cardiovascular Effects Are Associated With Chronic Kidney Disease in Type 2 Diabetes?” is sponsored by Bayer and is intended for physicians.

Here’s your host, Dr. Edgar Lerma.

Dr. Lerma:
Hello, and welcome to part 2 of this 3-part video series focused on the unmet needs of patients with chronic kidney disease and type 2 diabetes. I’m Dr. Edgar Lerma, and today I’ll be talking with Dr. Peter McCullough, a professor of medicine at Baylor University Medical Center in Dallas, Texas, specializing in cardiology. His research focuses on the role of CKD as a cardiovascular risk state. We’ll be discussing the role of overactivation of the mineralocorticoid receptor, or MR, in CKD.

Dr. McCullough, thank you for joining us here today.

Dr. McCullough:
Thank you for having me.

Dr. Lerma:
So before we begin, I wanted to take a look with you at some patient cases typical of what you and our listeners may see in practice. For our first patient, we have a 61-year-old man with type 2 diabetes, which was diagnosed 12 years ago. He has an estimated GFR of 48, a urine albumin-to-creatinine ratio of 994, and an A1c of 6.7%. He has a history of hypertension and had a myocardial infarction 6 months ago. His GFR declined by 12 over a 1-year period, and he is currently on metformin, insulin, statin, and maximum dose ACE inhibitor.

Dr. McCullough:
Well, based on his eGFR, this patient has CKD Stage 3. His UACR is very high, which places him at high risk for CKD progression.

Dr. Lerma:
I agree. Here, if we only use GFR to measure kidney function, we would miss the high risk for CKD progression as seen with high urine albumin/creatinine ratio values. Now, what about his risk for cardiovascular complications?

Dr. McCullough:
He has high blood pressure, and he had a myocardial infarction relatively recently, so I would consider him as having moderate to high risk for cardiovascular complications.

Dr. Lerma:
I would agree, but this case was pretty straightforward. What if we consider another patient I saw recently? This 48-year-old woman was diagnosed with type 2 diabetes about 7 years ago. Since then, we have gotten her blood pressure and glucose under control, but her kidney function is continuing to decline. What are your thoughts about why her CKD is still progressing?

Dr. McCullough:
That’s a great question, and I’m sure our listeners have seen their fair share of patients with a similar profile. As you mentioned in the first discussion, CKD progression is dependent on the combined effects of metabolic, hemodynamic, and inflammatory and fibrotic

factors. Managing elevated blood glucose addresses some of the metabolic effects, while managing elevated blood pressure addresses some of the hemodynamic effects. However, inflammatory and fibrotic factors are largely unaddressed by the standard of care. Inflammation and fibrosis in the kidneys can lead to declining kidney function as well as cardiovascular events.

Dr. Lerma:
Well put. And a major driver of this inflammation and fibrosis is the overactivation of the mineralocorticoid receptor, or MR, which will be the focus of our discussion today. Dr. McCullough, can you walk us through the role of the MR under normal conditions?

Dr. McCullough:
Sure. The MR is found in cardiac and vascular cells including cardiomyocytes, vascular smooth muscle, and endothelial cells and fibroblasts, and it is well known that the MR exerts direct effects on the heart, which is an important factor in our discussion.

Dr. Lerma:
Absolutely. And as you indicated, the MR can be found throughout the body, including the kidneys. What's the role of the MR there, Dr. McCullough?

Dr. McCullough:
The MR in healthy kidneys maintains the balance of various physiologic processes, including fluid, electrolyte, and hemodynamic homeostasis, appropriate cell responses, and regulation of inflammation.

Dr. Lerma:
MR overactivation has been implicated in a variety of disease pathways. Many of our listeners have heard about the role of MR signaling in cardiovascular diseases. One thing to note for our listeners is that MR expression is not fixed. The expression can be modulated in various disease states, such as diabetes, CKD with high albuminuria,cardiac failure, myocardial infarction, high blood pressure, vascular aging, or even cerebral aneurysms.

Dr. McCullough:
Exactly. In kidney and cardiovascular diseases, the MR pathway can become overactivated through increased expression or increased stimulation of the MR. As MR activators proliferate, the cell begins to produce proinflammatory and profibrotic proteins. These factors eventually lead to inflammation and fibrosis, which can lead to injury and structural changes in the kidneys, worsening kidney disease.

Dr. Lerma:
So let's talk a little more about the damage caused by inflammation and fibrosis. We know that an overaccumulation of unfiltered proteins puts stress on the kidneys. Thickening and scarring in and around the renal tubules caused by the proinflammatory and profibrotic proteins also decreases kidney function and increases the pressure. The structural damage of the kidney impairs the organ's functionality, ultimately resulting in end-organ damage. So with that understanding, let me turn to you, Dr. McCullough, to explain how this is linked to cardiovascular risk.

Dr. McCullough:
Inflammation and fibrosis lead to similar issues in the heart, but more importantly, the kidney damage caused by inflammation and fibrosis can also increase the risk of a cardiovascular event. In fact, patients with CKD and type 2 diabetes have a higher occurrence of comorbidities, such as stroke, coronary artery disease, and peripheral arterial disease than the patients with type 2 diabetes alone. Over a 10-year period, patients with CKD and type 2 diabetes were 3 times more likely to die of cardiovascular-related causes than patients with type 2 diabetes alone.

Dr. Lerma:
This is true. The FIELD study also found risk of cardiovascular mortality was significantly increased with greater kidney impairment.

Dr. McCullough:
Exactly, and we can look at the results in a little bit more detail. The 2 main tests to define CKD in type 2 diabetes are estimated glomerular filtration rate, or eGFR, and urine albumin-to-creatinine ratio, or UACR. Impaired eGFR and UACR are each independently associated with increased all-cause mortality and risk of cardiovascular mortality in patients with diabetes. In fact, in another study of the data from the Third National Health & Nutrition Examination Survey of over 15,000 individuals, showed that all-cause mortality more than doubled in patients with diabetes and albuminuria or impaired eGFR versus diabetes without kidney disease.

Dr. Lerma:
That's a great point, Dr. McCullough. We will expand on eGFR and urine albumin/creatinine ratio more in the next discussion in our episode, "How Do the Drivers of Chronic Kidney Disease in Type 2 Diabetes Play a Role in Patient Care?" Do you have any takeaways for our audience regarding MR overactivation in CKD and type 2 diabetes?

Dr. McCullough:
Yes. To summarize, under normal circumstances, MR signaling regulates electrolyte and fluid balance. However, under certain conditions, like type 2 diabetes, the MR becomes overactivated. Once overactivated, the MR drives the production of proinflammatory cytokines and profibrotic proteins, which can lead to injury and structural changes in the kidneys and the heart, worsening renal and cardiovascular disease. Patients with CKD and type 2 diabetes have a higher occurrence of comorbidities, such as stroke, coronary artery disease and peripheral arterial disease, than patients with type 2 diabetes alone. In fact, albuminuria and impaired eGFR, the measurements used to define CKD, are each independently associated with increased all-cause mortality and a risk of cardiovascular mortality in patients with diabetes.

Dr. Lerma:
Thank you, Dr. McCullough, for your insights on the cardiovascular effects of chronic kidney disease in type 2 diabetes.

Dr. McCullough:
Thank you for having me.

Dr. Lerma:
And to our listening audience, a reminder to look out for the third episode of this 3-part series focusing on managing the drivers of CKD in patients with type 2 diabetes. Thank you all for listening.

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.