



Transcript Details

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www.reachmd.com info@reachmd.com (866) 423-7849

The Hidden Threat: Transforming CKD Care Across the Diabetes Spectrum

Announcer:

Welcome to CE on ReachMD. This activity, titled "The Hidden Threat: Transforming chronic kidney disease Care Across the Diabetes Spectrum" is provided by Medcon International.

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Chapter 1

Dr. Fioretto:

Hi, I'm Paola Fioretto from the University of Padova in Italy, and I welcome you to this continuous education program on ReachMD.

Dr. Rossing:

And hi, I'm Peter Rossing from Copenhagen, Denmark, endocrinologist at Steno Diabetes Center.

Dr. Heerspink:

Hi, everyone, I'm Hiddo Heerspink. I'm a clinical trialist at the University of Groningen in the Netherlands.

Dr. Fioretto:

In the first chapter of this program, we are going to explore the hidden chronic kidney disease danger in patients with diabetes. And I would like to start by hearing from a patient.

Patrick:

Hello. My name is Patrick Gee, and I currently live with diabetic kidney disease. And my journey began in 2003 when I was diagnosed with type 2 diabetes. And from 2003 to 2013, my endocrinologist had prescribed 2 forms of insulin to help me manage my diabetes.

I thought everything was going pretty good up until April of 2013 when I was told at that time that I was diagnosed at stage 3b of end-stage kidney disease, and I only had 30% to 35% kidney function. Now, imagine going to your physician and you are just finishing an appointment and you walk out to your car. And as I'm getting ready to get in my car, my doctor runs out and she says, "Hey, Patrick, I have to tell you that you're at stage 3b and that you have between 30% to 35% kidney function."

I didn't know how to take the news. A myriad of emotions was going on with me. I didn't know if I was going to die. My doctor told me in a less-than-compassionate manner. It was never told me that, "Hey, we can do therapy so you can understand it. I can help you with this." Nobody had even told me that diabetes was the number one cause of kidney disease. So you can imagine trying to get in my car and process this and to go home and tell my family this, not knowing if it's a death sentence or not. And the only other thing that she





said was, "You're going to have to talk to a nephrologist." At that particular time, I didn't even know what a nephrologist was.

But 2 weeks later, talking to the nephrologist, the nephrologist told me, "Yeah, Patrick, eventually you are going to go on dialysis. But if you could abstain from chocolate, dairy products, and nuts, it can slow down the progression."

So within the same year—actually it was December 1, 2013—I actually began peritoneal dialysis, still trying to manage my type 2 diabetes, as well as doing peritoneal dialysis.

And in the end, in 2017, I ended up getting a kidney transplant and have better learned through this entire process of how to manage my type 2 diabetes as well as my kidney disease.

So thank you for allowing me to share that story.

Dr. Fioretto:

As you have seen from this case, frequently the diagnosis of chronic kidney disease is done very late. The patient was shocked by hearing that he had advanced chronic kidney disease nobody ever told him about. And I believe that early diagnosis is extremely important in chronic kidney disease, given that we have treatments today able to slow progression and to improve the prognosis of these patients.

Now, chronic kidney disease is the most common complication of patients with type 2 diabetes, affecting 40% of these patients. And patients with chronic kidney disease have a very increased risk to have cardiovascular disease and also heart failure. The importance of early detection, therefore, is extremely important.

So, Peter, can you tell us how can we improve early detection of chronic kidney disease in these patients?

Dr. Rossing:

It's important to realize that there are no symptoms associated with having kidney disease until the very late stages, and that's why we need to rely on screening or regular assessment of kidney function or eGFR and albuminuria testing. So it's simple and it's once a year. You test albuminuria, and you test kidney function with creatinine and calculate eGFR. And thereby, you can evaluate the risk whether you have kidney disease in early or in more advanced stages. And as you said, this is super important because we have treatments that can stop the progression of the disease and the associated cardiovascular disease, which is so prevalent. So the increase in markers of kidney disease, albuminuria and GFR being low, is associated with kidney disease progression but also mortality and cardiovascular disease. So it's really important markers for kidney disease and, thereby, the initiation of treatment, but also markers of other complications related to CKD and diabetes.

Dr. Fioretto:

The mechanisms involved in the progression of chronic kidney disease in diabetes are complex. They include metabolic factors; of course, patients with diabetes have hyperglycemia. They involve also hemodynamic factors. It is well known that patients with diabetes have an increase in intraglomerular pressure and glomerular hyperfiltration. And more recently, an important role for inflammation and fibrosis has been recognized as an important progression promoter. In this regard, mineralocorticoid overactivation has an important role in that when there is an activation of this system, there is more inflammation and fibrosis.

In the last years, 2 important classes of drugs became available to tackle these mechanisms. One are the SGLT2 inhibitors, which improve glycemic control, but especially they have hemodynamic effects, decreasing the increase in intraglomerular pressure. And then we have one new nonsteroidal mineralocorticoid receptor antagonist, which is finerenone, that has been shown to have important effects in slowing progression of chronic kidney disease, and that's because it's able to decrease inflammation and fibrosis.

Dr. Heerspink:

And so we have new interventions that do not only target inflammation and fibrosis but also reduce albuminuria. And so with these new interventions, we can now screen for albuminuria early, treat patients with safe and effective treatments that reduce albuminuria in order to slow the progression of cardiovascular and kidney disease.

Dr. Fioretto:





Thank you, Hiddo. This is very important because in the past, even if we were screening and diagnosing chronic kidney disease, we had nothing to offer to our patients to improve prognosis.

Dr. Rossing:

Yeah, and maybe just to highlight also that it's really important to screen again. I want to, before we move on, say that we need to screen. And there are several campaigns trying to urge physicians to really screen for this. And European Renal Association has this ABCDE rule: test for albuminuria, test for diabetes, but also blood pressure, cholesterol, and eGFR.

So I think trying to make it simple to remember to screen. In general, people are good at screening for eGFR, but albuminuria screening is often forgotten, unfortunately, because it's such a good marker, as Hiddo has demonstrated in many trials. And as we have seen in many etiological follow-up studies and in trials, albuminuria indicates risk, and if you reduce albuminuria, you are doing something good.

Dr. Fioretto:

Sure, I agree.

In summary, in this first chapter, we discussed the burden of chronic kidney disease in diabetes, very common complication. We discussed about the risk of cardiovascular disease that these patients with chronic kidney disease have very high risk. We discussed on the importance, fundamental for the proper treatment of the patients, the early diagnosis of chronic kidney disease by measuring albumin in the urine and eGFR, very simple creatinine in the plasma.

We also discussed on the mechanisms involved in the progression of chronic kidney disease in patients with type 2 diabetes and the availability of treatments that tackle these mechanisms. And I'm referring to SGLT2 inhibitors and to finerenone.

In Chapter 2, we will focus on the pillars of chronic kidney disease management in patients with type 2 diabetes.

Chapter 2

Dr. Fioretto:

Welcome back. In the first chapter, we discussed the hidden chronic kidney disease danger in diabetes. Now, let's turn our focus on the management of patients with type 2 diabetes and chronic kidney disease.

Peter, I understand you want to start with a clinical case.

Dr. Rossing:

Yes, and thanks a lot. I have one of my patients, John, typical with type 2 diabetes. Feeling well, enjoying his life. But once he had his lab done, he was diagnosed, we can say, not only with diabetes but also having chronic kidney disease. It turned out he had impaired kidney function. He had increased albuminuria. He was treated by his general practitioner with an angiotensin II receptor blocker, which was what was available at that time for management of kidney disease and hypertension. And with diabetes drugs, metformin and sulfonylurea.

He was also receiving a statin, and then he was referred to me a couple of years later because now there was further progression. He had lost kidney function. He had increased albuminuria, so now GFR was 54, and his albuminuria was more than 300, which is our threshold for severely increased albuminuria, and still on the same treatment. And the discussion is, of course, then what can we do to help a person like John?

He's also having obesity, in addition to the hypertension, diabetes, kidney disease. So very typical for the type of people we see with diabetes and chronic kidney disease.

And you can say a case like him is actually, he could fit almost in all the trials we have had recently, where we have seen a new treatment being developed for management of chronic kidney disease and diabetes. And these trials with SGLT2 inhibition, with the nonsteroidal mineralocorticoid receptor antagonist finerenone, and with the GLP-1 receptor agonist semaglutide, have added to our guidelines and to our understanding and given us more opportunities for how we can really address a person like John and help him to





stop the progression of kidney disease, reduce his risk for cardiovascular disease, and also reduce his risk for dying of his diabetes and kidney disease.

And you can say the guidelines would say that the foundation would be RAS blockade, because that has been from trials, more than 25 years ago, the standard of care. But now we have seen that SGLT2 inhibition provides good data on kidney and cardiovascular protection, as we discussed also in the previous chapter.

We have seen in trials with finerenone that there's less progression of cardiovascular disease, less progression of kidney disease. And we saw most recently with semaglutide in the FLOW trial, there was also a benefit. And that has entered the most recent guidelines.

So we have a lot of opportunities. The important thing is John would never know this if he had not been screened and tested as we discussed previously. So we need to screen and then add these treatments into the armamentarium of people like John.

Dr. Fioretto:

So, Peter, I have a question. Now, John was diagnosed late because when he came to you, he had already proteinuria, low GFR, so very high risk of progression. And you mentioned that we have treatment options, and the guidelines recommend, in addition to RAS blockade, SGLT2 inhibitors, finerenone, and now also semaglutide.

So in order to be more effective for these patients who already lost a lot of time before getting appropriate treatment, how do you feel about starting some of these therapies together?

Dr. Rossing:

Well, that's a good question and the trials were done in parallel, so they didn't really answer what to do. But recently we got the CONFIDENCE trial where an SGLT2 inhibitor was combined with finerenone and started at the same time in normal treatment doses. And actually, that went very well because we could see in that trial that there was added effect on albuminuria, so 30% more reduction when you give the combination of an SGLT2 inhibitor and finerenone compared to one of these agents alone. But you could also see that it was safe in the sense there is a small dip in GFR, as you would expect. The combination of the SGLT2 inhibition and with finerenone, but nothing more than that. Events with hypotension or events with acute kidney injury was very rare. So you can say we could safely start 2 agents at one time.

Dr. Heerspink:

And, Peter, sometimes in clinical practice, they ask us the question, should we sequence them quickly after each other, or should we start simultaneously? What would you recommend or would you advise?

Dr. Rossing:

Yes, thanks. Because as you say, this is a common question. And in CONFIDENCE, it was started simultaneously. If you would prefer to postpone and do it sequentially within a month or so, that's also fine. But don't postpone the increase 6 months or 12 months. So it depends a little bit on what's possible in your setting. But the effect of these drugs is very quick, so if we delay it for 6 or 12 months, we actually lose an opportunity, so we shouldn't delay this combination too much.

Dr. Fioretto:

So I think, Peter, that your setting is peculiar because the Steno Diabetes Center is one of the best centers for diabetes care in Europe. But in the routing setting, it's not easy to see the patient again in 1 month. So I believe that now that we have information on the simultaneous initiation of 2 agents being safe and effective, that is very helpful in the clinical practice.

So in this Chapter 2, we went through the drugs that are recommended from the guidelines for the management of patients with type 2 diabetes and chronic kidney disease, and we also discussed the possibilities of using them together and even to start them simultaneously in order to obtain a faster response in our patients. Because I think it's also important for the patient to see the results. When they see that albuminuria is decreasing, of course they are very happy.

In Chapter 3, we will change our discussion and move into the challenges that patients with type 1 diabetes and chronic kidney disease have.





Chapter 3

Dr. Fioretto:

Welcome back. Now, we are going to change our focus and move to consider the patient with type 1 diabetes and chronic kidney disease.

This is a very important topic, and I would like to ask, a patient with type 1 diabetes, Uros, to tell us about his history.

Uros:

Yeah, thank you. So people with type 1 diabetes face similar complications as people with type 2. Although the incidence rates obviously may differ, we have a feeling of being left behind in some of these areas where novel treatment is given and developed mainly for people with type 2. But unfortunately, even with our high incidence rates, we are not given the same treatment. And I think that really needs to change.

We are aware of the complications. We are aware that we are constantly reminded by our healthcare professional team that we must do everything that we can in our blood glucose management to avoid these complications. But then, if those complications do arise, then we are faced with a very bad moment that we do not get the access to the best therapies that exist

Dr. Fioretto:

Uros, I perfectly understand your point. And I think that despite the fact that glucose control is very important, we have seen that there are other mechanisms involved in the kidney to cause chronic kidney disease and to influence the progression of chronic kidney disease that have nothing to do with glycemia.

I think that it would be important to have the opportunity to offer additional therapies, not only glucose control, blood pressure control, also to patients with type 1 diabetes who are much younger than type 2.

So, Uros, I have a question for you. What was your reaction when you were diagnosed with type 1 diabetes

Uros:

It is a life-changing moment for sure, for everyone diagnosed with type 1. The first feeling is fear and uncertainty of what is about to happen and how it will impact our lives. But I think from that first moment onwards, if you get to grips with your condition, if you follow the guidelines and, most importantly, if you connect with your peers who have the same condition, I think you are bound to get more improvement and better results than just doing it on your own.

We are consistently reminded by our healthcare team that complications are potentially there, that there are risks of developing complications, but we focus mostly on just our glucose management. And we need to get away from that silo because as you already mentioned, it's not just about glucose management. There are other risk factors involved as well.

So I think we need to work on, first of all, the awareness of individual complications, because primarily, the healthcare team doesn't seem to speak too much about individual complications. They frighten us with air quotes of complications in general, but we must be aware of the different types and what can we do to prevent each one.

Dr. Fioretto:

Yeah, so I think this is very important.

So, Hiddo, can you tell us something? Do we have any hope? Is there anything going on in order to address this important problem

Dr. Heerspink:

We shouldn't leave these patients behind. And we have to develop new therapies for patients with type 1 diabetes because their risk is as high as patients with type 2 diabetes. Fortunately, we are developing new therapies for people with type 1 diabetes.

One of the clinical trials, which is FINE-ONE, is a clinical study in people living with type 1 diabetes and chronic kidney disease that will assess the efficacy and safety of the nonsteroidal mineralocorticoid receptor antagonist finerenone in these patients. And I'm very





thrilled to announce that the study is already almost completed. We have followed these patients for 6 months. The endpoint is albuminuria reduction, because you may remember from our first episode that albuminuria is an important risk marker for cardiovascular and kidney disease and that therapies that reduce albuminuria will in the long term also confer cardio and kidney protection. That's why albuminuria in this study is the endpoint, and we hope to present the data in the very near future.

And if positive, this would mean that for the first time in 30 years, we have developed a new therapy for people with type 1 diabetes and chronic kidney disease. And I believe that is a major breakthrough and also an incentive for other people to develop new treatments for these high-risk individuals with type 1 diabetes and chronic kidney disease.

And thus, Uros, I hope that with the completion of the FINE-ONE clinical trial, we have addressed the concerns that you have expressed and that we are not leaving patients with type 1 diabetes behind.

Uros:

Thank you for saying that. I really do hope that we will see some improvements. We are now doing the research, but we need to also focus on the implementation afterwards that we really don't get left behind, so that first we try to avoid CKD in the beginning, but if CKD does develop, that we actually have good treatment options for those people.

Thank you

Dr. Fioretto:

This has been a very exciting conversation, especially thanks to the presence of a patient with type 1 diabetes. And I'd like to thank all of you for listening to this program and also to the speakers for joining us today.

Dr. Heerspink:

I also would like to thank all the audience for listening to us. Stay tuned. In the near future, we'll see much more about new therapies for type 1 diabetes, and I'm sure that we also will not forget type 2 diabetes and develop even better combinations in the future.

Announcer:

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