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https://reachmd.com/programs/cme/case-based-approach-optimizing-cardio-kidney-metabolic-outcomes-in-individuals-with-t2d-ckd/29906/

Released: 10/31/2025
Valid until: 10/31/2026
Time needed to complete: 15 minutes

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Case-Based Approach: Optimizing Cardio-Kidney-Metabolic Outcomes in Individuals With T2D & CKD

Announcer:
Welcome to CE on ReachMD. This activity, titled “Case-Based Approach: Optimizing Cardio-Kidney-Metabolic Outcomes in Individuals With type 2 diabetes & chronic kidney disease” is provided by Medcon international.

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Dr. Agarwal:
Hi, I'm Dr. Rajiv Agarwal, professor emeritus, Indiana University School of Medicine and staff physician at the VA Medical Center in Indianapolis, Indiana, USA.

How we detect CKD in patients with type 2 diabetes and what is the optimal treatment approach for these patients is what we are going to learn through a case today.

This is CE on ReachMD, and together with me is Dr. Cos.

Dr. Cos:
I'm Dr. Cos, associate professor at University Autonomous in Barcelona. I'm a GP in practice. So for me, it's also an honor to be in this program today.

Dr. Agarwal:
We're going to start with a case—a case that you might see in practice. 57-year-old male executive with a history of long-standing hypertension and obesity being treated with losartan 100 mg once a day and amlodipine 10 mg once a day. He presents to his primary care physician with chest pain, BMI is 29 kg/m^2, blood pressure 129/78, and he has trace pedal edema. He is referred to cardiology. He undergoes a treadmill test which is positive for inducible ischemia. He's taken for cardiac cath, which reveals significant right coronary artery disease. A stent is placed, and he is discharged.

In the second week, he follows up with his primary care physician. He gets a routine screening which identifies dyslipidemia and new-onset type 2 diabetes. He's placed on a statin, aspirin, and his hypertension is managed without changing any medicines to his regimen. His diabetes is treated with metformin and empagliflozin 10 mg once a day.

The following year he returns for a follow-up visit. His creatinine is 1.2; his eGFR is 67. He is discharged with no further action. Blood pressure 126/72, BMI 29.6, HDL 45, LDL 74.

Eight months later, he presents to the emergency room with a myocardial infarction. Upon admission, a dipstick test is positive for proteinuria, a subsequent urine albumin-to-creatinine ratio confirms significant albuminuria at 700 mg/g.

So here's a patient who really had a myocardial infarction, who had type 2 diabetes. And the question is, who do we screen for chronic kidney disease? Clearly, his eGFR was more than 60, so he didn't really qualify for diagnosis of CKD in a patient with type 2 diabetes, but he never had screening for UACR or dipstick or whatever at the first visit when he should have had. All the guidelines say the same thing—that screen the patient for albuminuria at the time of diagnosis and at least annually thereafter.

So, Dr. Cos, in your practice, would you think that this patient would have been screened for albuminuria for a diagnosis of CKD?

Dr. Cos:
Yes, of course. This is a kind of patient we normally could see in our practice, in the primary care setting. Of course, it's a patient that, when came, already had an important vascular disease, has been admitted to the hospital for a coronary artery disease. And I think that at 2 weeks after, it was this onset of type 2. And any patient that will visit our clinic that has been diagnosed by type 2 requires some assessment. And one of the assessments we are doing is exploring what's going on in the kidney. That means to do eGFR estimation, a glomerular filtration rate calculation, and also allow us to know what is the function of the kidney and also if there's any damage now running in the kidney as well, so that for our UACR are the parameter we are using normally. But of course, that is bringing 2 different dimensions of what is going on in the kidney.

So of course, any patient we have in our clinic at the diagnosis moment, and also in the follow-up, we are doing that kind of testing. So I think it's appropriate to be considered, probably at the beginning, to do kind of testing, a baseline. That is an important aspect to keep in mind.

Dr. Agarwal:
So you raise 2 very important questions. One is the assessment of kidney function, which is through the GFR, and the other one is to assess kidney injury or possibly endothelial dysfunction through the assessment of UACR.

So if you have a lot of UACR, say more than 300, then it's possible that patient has some kidney injury. If you're in the microalbuminuria range, what we call A2 albuminuria, it could be more endothelial dysfunction.

Dr. Cos:
Correct.

Dr. Agarwal:
And what you're saying is that we should have screened them right at the get-go.

Dr. Cos:
For sure. Because when you're screening it's because you are understanding something behind that screening, and that means that allows you to stratify what's the risk of that individual you have in front of you, and it means that probably your actions must be different according to what you are detecting. So screening, why? Because we have a reason to do something; because we have solutions.

Dr. Agarwal:
So it's very interesting. What you say is that albuminuria, we should be screening for in everybody who has new-onset diabetes. This patient wasn't.

Before 2019 we only had ACEI and ARBs. And yes, we have had these guidelines for screening of UACR for at least a few decades now. But since 2019 we have built more and more evidence that we can impact the lifetime course of kidney disease and cardiovascular disease, in particular in these individuals who we can detect early, right?

Now that we have detected CKD in this individual—he has 700 mg/g A3 albuminuria—let's talk about the treatment in our case, who has both type 2 diabetes and CKD. So some people says, "Oh, the patient is on statin, aspirin, SGLT2 inhibitor. It's pretty good. He's receiving the standards of care, and why bother with more medications? They're not going to make that much of a difference."

So do we have new evidence now that can make an impact on this individual?

Dr. Cos:
I think that, of course, the kidney is something that for primary care physicians, we don't feel really aware about it. I think that having solutions available, it provides more sense to be more focused on the kidney.

The story with the SGLT2 inhibitors is a clear example—something that was considered for management of type 2 diabetes, and then you observe, in these cardiovascular outcome trials, benefits in the kidney—something it was opening new windows, and, of course, new studies has been designed just to provide proper answers of that.

At the same time, we know about the GLP-1 receptor agonists. Injectables at the beginning, we now have oral formulations. We have dual peptides. So we have a lot of things. A lot of them include in their trials what's going on in the kidney in those participants. And we know there are also benefits on the persons that have been participating in the trial.

So this is bringing evidence about the benefit of that, and this is translated into the different guidelines and algorithms, also in the guidelines in the primary care.

And also we have this, the finerenone as a compound that is also having an impact. It's also very relevant because also project that benefits in the kidney. So now, of course, it's a point that probably those clinicians in the primary care setting that were not really being familiar with that medication or with that beneficial effects probably be more tailored and more educated how to understand how that medications could be beneficial for those patients that are in that situation.

So it's just closing the loop. We are screening for something because we have a solution we can use in those individuals.

Dr. Agarwal:
Very good. So 2 things that we see—we have 4 pillars of care. Two of them are medicines to treat diabetes, and two of them are blocking the renin-angiotensin-aldosterone system. Right? It turns out that both of the diabetes medications were kind of discovered accidentally, because the regulators mandated trials to show cardiovascular safety, and lo and behold, we actually have better safety than placebo, which means that they are protective. So that we weren't really designing these trials to show benefits; we were simply trying to design it to show no harms, because of the prior things. And we show benefits on both the kidney now.

Now, finerenone was different because it was deliberately designed to look at the addition of this molecule on top of the existing therapies to show. And now we have the embarrassment of riches.

So the question we get asked often is: why simultaneous start of a SGLT2 inhibitor and finerenone? And this is on top of ACE inhibitors and angiotensin receptor blocker therapy. And the answer is quite simple. Where we have multiple therapies that have to be added, if they are added sequentially, people simply don't get on all those therapies. We know this from hypertension combination therapies. We know this from heart failure with reduced ejection fraction, where there are multiple therapies to be added.

For example, in people with heart failure with reduced ejection fraction, the guideline is that use some of all instead of all of some before the patient gets out of the hospital.

But we have no such data in people with chronic kidney disease with type 2 diabetes and albuminuria. So we said that if we use simultaneous therapy, can we demonstrate greater efficacy of starting them together? And can we also demonstrate safety? And now we have done a trial called the CONFIDENCE trial, in which we randomized people to either finerenone alone or empagliflozin alone, or both. All these people have type 2 diabetes and kidney disease, albuminuria in the range of 100 to 5000, eGFR between 30 and 90. And what we are looking at is the change from baseline in albuminuria from baseline to day 180. Compared to finerenone alone or empagliflozin alone, we see between a 29% to 32% greater reduction in UACR when we use the combination from the get-go.

There is an initial GFR dip about 5-6 mm with the combination therapy. And this is expected because both these treatments reduce blood pressure about 7.5, and the GFR dip is what you would expect, just like if you're using a beta-blocker, the heart rate reduction is expected. The reduction in eGFR is an expectation when you start finerenone and SGLT2 inhibitor together. It's not a reason to stop therapy unless the patient has symptomatic hypertension or has a clinical acute kidney injury.

So when you're starting these therapies, you have to be cautious and sort of monitor the blood pressure in these people on a continuous basis to make sure that, because these patients are getting hypertensive, they are not also experiencing kidney failure. But if we monitor the blood pressure, you monitor the UACR, we can see a 30% reduction in UACR at day 14, which is really the ADA guideline of having at least 30% reduction in these individuals. Half the patients will have at least a 30% reduction in 2 weeks, which we have never seen in any clinical trial before.

So there's an advantage of starting combination therapy simultaneously. But what it also tells you is it's never too early to start the second drug. You don't have to wait a month or two or whatever to start the two drugs together.

In this particular individual, who we discover a year later that he had 700 mg, it's possible that if he had used these combination therapies right from the get-go, we could have reduced his risk of cardiovascular disease progression. And at least from the finerenone trials, the FIGARO trial in particular, we show that there's a reduction in the risk of cardiovascular death, of myocardial infarction, and heart failure hospitalization in these individuals who have type 2 diabetes and CKD.

Now some people ask us whether GLP-1 RAs act independently. So we've really never done any trials to look at GLP-1 RA on top of 3 pillars of care. So what we have done best is, in CONFIDENCE trial, 23% of the people were on GLP-1 RA, and the remaining were not. And we asked the question whether the GLP-1 RA modified the treatment response in terms of reduction in UACR, or the adverse effects or the serious adverse events, and the answer was neither was modified. In other words, GLP-1 RAs seemed to be acting independently of the other 3 treatments.

So it goes to show that in the real world, if we combine these therapies early, we can reduce the lifetime burden of cardiovascular disease and kidney disease progression.

So before we wrap up, let's each offer a final take-home message. Dr. Xavier, what do you hope our listeners will leave with today?

Dr. Cos:
I think it's important to keep strong messages, and one is why we have to screen. And I think it's clear in what our dialogue has seen explained.

The second is how to do it, okay? And also we have to understand that we have 2 parameters that are going to provide different information that are going to be complementary in understanding what is the stratification of the risk of that individual.

So I think it's we are doing those 2 aspects, because at the end, we are detecting individuals with risk, and then we have solutions that have just been mentioned.

We have to consider, in our formulary, to use it in clinical practice. But at the same time, it is very key, in my opinion, that probably we are not really familiar of these compounds. That, I think, it invites us that probably we have to have better communication with those colleagues that are around us—maybe the kidney units, the nephrologists we have around—and have better communication in terms to understand how we can invite my patients to start using that solutions. Because I know how these compounds are working, and I can be embracing them in terms to start using in their management in daily basis. So I think that is also inviting you at that moment, I mean, representing a kidney specialist, that will be together in that journey trying to help our patients living with that condition.

Dr. Agarwal:
So, great points. I look at the awareness of blood pressure and cholesterol and the cessation of smoking, and we look at the A1c in diabetes, but there are very few people who know UACR or proteinuria or dipstick proteinuria. There's sort of the awareness of it is not as high as blood pressure, cholesterol, smoking. So that's one piece of it.

Second part is that if we impact the UACR early, we can have lifetime benefits. One way to think about it is where there is smoke, there is fire. And what UACR is telling us, there's smoke, and the fire is in the kidney and the cardiovascular system. In the past, we only had ACE and ARBs, but now we have three other therapies to quench that fire, and I think adding them early to let that fire not burn the cardiovascular and the kidney system down is really the key message.

And that's all the time we have today. So I want to thank our audience for listening, and thank you, Dr. Cos, for joining me and sharing all of your valuable insights and expertise.

Dr. Cos:
Thank you very much.

Announcer:
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