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# A Practical Look at Cardiorenal Protection for CKD in T2D: Applying Recent Data

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**Dr. Lam:**
Achieving optimal outcomes when treating patients with chronic kidney disease [CKD] in type 2 diabetes remains challenging and requires a multidisciplinary approach to prevent progressive renal dysfunction and cardiorenal events. What are the latest evidence and guidelines telling us about how to manage these patients with nonsteroidal mineralocorticoid receptor antagonists, or MRAs, in the real world?

Well, this is a CME on ReachMD. And I'm Dr. Carolyn Lam.

**Dr. Taub:**
And I'm Dr. Pam Taub.

**Dr. Caramori:**
And I am Dr. Luiza Caramori.

**Dr. Cebrián-Cuenca:**
And I am Dr. Ana Cebrián.

**Dr. Lam:**
Thank you so much, Luiza and María, Pam, for being with us today. Pam, could we start with you? Could you perhaps tell us about a case of early CKD in a patient with type 2 diabetes and what the latest evidence says and how that impacts your therapeutic choices?

**Dr. Taub:**
Well, I'd love to. So let me tell you about a real patient, one of my patients that I followed for many years. She is a 73-year-old woman with long-standing diabetes. Her diabetes was diagnosed about 15 years ago. She also has hyperlipidemia, and she presents for routine follow-up. And she sees me as a cardiologist because she has a family history of early coronary artery disease, and she has an elevated lipoprotein A. So her current medication regimen is rosuvastatin 10 mg daily. For her diabetes, she's on metformin 1,000 mg twice a day. She's also on the GLP-1 receptor agonist dulaglutide at 1 mg per week. And we obtain recent bloodwork and that reveals that her hemoglobin A1c is 7.5. Her potassium is 3.9, and her creatinine is normal at 0.64, and her calculated eGFR [estimated glomerular filtration rate] is greater than 90. I also check a UACR [urine-albumin-to-creatinine ratio] to look for microalbuminuria because of her long-standing diabetes. And that is a little surprising. It's elevated at 147. And so she's then started on an SGLT2 [sodium-glucose cotransporter-2] inhibitor, empagliflozin, but 2 weeks later, she develops a urinary tract infection which I treat. Then 4 weeks later, she develops a genital mycotic infection, which I also treat, but she discontinues the medication and doesn't want to continue with

the SGLT2 receptor class.

So then we discuss other options in terms of what can I do to prevent her progression of renal disease, and I start finerenone 20 mg daily because her potassium is 3.9. It's in a range where you can start with a higher dose. And then 3 months later I check a UACR, and it's nice to see that decrease from 147 mg/g to 96 in a short period, very consistent with what we've seen in clinical trials with use of a nonsteroidal MRA.

**Dr. Lam:**
Luiza, what do you think about this case? Would you have done different?

**Dr. Caramori:**
Yeah, no, I think that's quite interesting. And this patient, of course, it's very similar to many of the patients we see in clinic, long-standing diabetes with some microalbuminuria. And as we all know well, many times cardiovascular disease is not as thought of in females, and we need to be careful with that. Sometimes we think about risks, and we think about male patients at high risk for cardiovascular disease, which they are, but we need to keep in mind that our female patients, especially those with diabetes, are also at very high risk for cardiovascular disease. And I think that increased UACR may also be a marker for this increased risk, as Pam was alluding to.

We do see, unfortunately, some patients who cannot tolerate the SGLT2 inhibitors. And in that regard, some patients also have a urinary incontinence, and that makes things a little bit more complicated. I have a patient very similar to the one who Pam presented who has urinary incontinence, and there is no way we would use SGLT2 inhibitors on her. So it's great to have other options that we can use and still get the beneficial effects in terms of cardiac and renal protection for these patients.

**Dr. Lam:**
Well, you know what, Pam, I'm actually really admiring the way you managed this case, because as a fellow cardiologist, I'm not so sure I would have checked the UACR. So I'm humbled with the finding that you can have a completely normal eGFR and have proteinuria, which indicates you need to do something about it. So kudos that you did that. But I know that that's also based on the new data. Right?

So, Ana María, could you perhaps tell us a little bit about that new data and why us cardiologists need to start learning to check UACR?

**Dr. Cebrián-Cuenca:**
Thank you. Cardiologists and also family physicians, as me as a primary care physician, I have also many problems because we are not thinking enough about the risks the patients have because of the kidney, not only the eGFR, we must also ask for the albuminuria. And that is a missing value, and I think is general for all the specialists. And it's very important, yes, to have both eGFR and also albuminuria to assess properly the risk of this patient. You will present a patient in stage 1 or 2. And these patients are at high risk of cardiovascular events. And we must ask also the eGFR and also the albuminuria. There is more than tenfold higher risk of cardiovascular event in patients with chronic kidney disease in stage 1 or 2 than patients without chronic kidney disease. And that is a crucial aspect. We have to ask for the albuminuria because it's a cardiovascular risk-dependent value.

**Dr. Lam:**
I noticed, Pam, too, that you commented on, you know, being sure to look at the potassium too. And I think one thing that we need to always remember is the nonsteroidal MRAs still need us to be responsible in looking at the potassium as well. Could I just ask your quick thoughts on sort of how you manage that?

**Dr. Taub:**
So this patient's an example of someone who had a potassium of 3.9. And so per kind of the expert consensus guidelines on how you practically manage these patients, that's a patient that could be easily started on a higher dose of finerenone at 20 mg. But if you have a patient that has a history of hyperkalemia, or the potassium levels are elevated in any historical context, maybe it was 6 months ago, or if their current potassium level is over 4.5, you could be more conservative and start at 10 mg, recheck the potassium in about a month, and then you can increase it to 20 mg. So having 2 doses really gives you flexibility because a lot of these patients have a lot of other medications such as ARNIs [angiotensin receptor-neprilysin inhibitors], ACE [angiotensin-converting enzyme] inhibitors, ARBs [angiotensin receptor blockers], where they can have higher potassium levels.

**Dr. Caramori:**
So I think that another point, Pam, on your patient that's quite important is that the eGFR is normal, right? So with the eGFR up over 90, it's very unlikely that the patient will develop hyperkalemia, and that allows us to start at the higher dose, as Pam did on this case. And I completely agree that we don't see as often patients being checked for urinary albumin, in general, even among endocrinologists, even though it has been on the guidelines for, you know, over a decade. But certainly, seeing our colleagues from cardiology also checking urinary albumin, I think that's going to help us identify these patients at high risk, especially now that we have therapies that can reduce

the renal and cardiovascular risk. So this is really, really important. Look for these patients, identify these patients, and give them the therapies as Pam was doing with her patient here.

**Dr. Lam:**
Thank you, Luiza. I think we needed a real, real good reminder. And if I could also share with everyone, super excited – at the ESC [European Society of Cardiology], we released our 2023 update of the heart failure guidelines. And there's a focus on prevention of heart failure and a new, strong recommendation that in patients with type 2 diabetes and CKD, we should be considering finerenone. So, you know, I think this is bringing it sort of close to our hearts as cardiologists now, and so I will change my ways. So thank you, Luiza.

And perhaps could we now hear about on the other spectrum of CKD. Luiza, could you share a patient who has established CKD also in type 2 diabetes, and perhaps let us know how the new guidelines may impact your treatment approach and also how this approach may differ from the case that Pam had shared?

**Dr. Caramori:**
Sure, thank you. So this is also a patient of mine, and he had been my patient for several years. This gentleman is actually a physician, and he's a little bit younger than the patient that Pam presented. But he has had diabetes so for over 20 years. He used to be quite overweight, has lost some weight and is working on that. In addition to his diabetes, he has hypertension, he has atrial fibrillation, hyperlipidemia. And as I mentioned, he is still obese. So he has been treated with several medications over the course of these many years. And currently he is on an extended-release formulation of metformin that he takes 1,000 mg per day. He is on irbesartan, that's an angiotensin-receptor blocker that he takes once a day. He's also on an SGLT2 inhibitor that we started quite a while back, and he's on metoprolol because of his AF [atrial fibrillation], and he's also on semaglutide because he was really struggling to lose weight. He's doing a great job with his diet and exercise, and he has been really great on that. So we added a GLP-1 RA to facilitate weight loss for him. And he chose to use an oral formulation for this agent at the time we started. He is also on edoxaban, and he still takes some insulin to control his diabetes. In addition to that, because of his hyperlipidemia, he is on 2 lipid-lowering agents that he takes daily. His blood pressure is reasonable, not ideally controlled, 134/82, with a BMI of 36 when I start seeing him. His glycemia is very well controlled with an A1c of 6.8%, his LDL is at 69, his triglycerides are 96, potassium is great, 4.4, and with a creatinine of 1.5, this brings his estimated eGFR to 51. And his urinary albumin-to-creatinine ratio is actually 405. So this came down over the years with the therapies that we have started with. His is still, you know, with an elevated UACR, that brings him to the macroalbuminuria protein or proteinuria or high albuminuria range. We have all these new names now, but that's in a high-risk category for this patient with increased urinary albumin level and his eGFR of 51.

So he also has some other things that are important here. His dad died years back from end-stage renal disease and he had type 2 diabetes. And he really wants to do all that he can to reduce his cardiorenal risk, which, of course, is understandable. Not always a patient will come to you with this comment: “I want to reduce my risk of dying from heart disease or having a kidney problem.” But this patient, you know, because perhaps he is in the healthcare, he had this request. And he also asked me if we could look at his medications and try to reduce a little bit the number of pills that he was taking throughout the day. So we know he has stage 3a CKD. He has albuminuria, and he has these multiple comorbidities. And although he is tolerating his medications well and his blood sugars are well controlled, his lipids are reasonable, I think we can do more for his cardiorenal protection. So we have a longer discussion. And of course, with the results of FIGARO, FIDELIO, FIDELITY program, as Carolyn mentioned earlier, we talked about using a nonsteroidal MRA, and he was interested in using finerenone. Because his eGFR is lower than 60, we started him on 10 mg daily, we checked potassium 4 weeks later, his potassium was still great, 4.6, there was a little normal variation, his estimated GFR, that was 49, we went up to 20 mg, and he did great. We checked again a few weeks later, and his potassium was at 4.7. So we continued him on the 20-mg dose.

He came back again 3 months after this new increase on dose, and he was doing great. But then he asked to reduce the number of drugs that he was taking if possible. So we start to combine some of his drugs.

So he's doing well. His blood pressure now is at target. He lost more weight and now his BMI is in the overweight category, no longer under obesity. And importantly, with the addition of finerenone, his urine albumin-creatinine ratio that was 405 dropped to 273. So a significant decline, a little bit over 30%. And that's what we usually see with these agents on average, of about 30%. So he's really doing well.

So a bit more complex of moderate to advanced disease, more complications, and we do see quite a lot of these patients in the clinic as well.

**Dr. Lam:**
And for those just tuning in, you're listening to CME on ReachMD. I'm Dr. Carolyn Lam, and here with me today are Dr. Pam Taub, Dr.

Ana María Cebrián, and Dr. Luiza Caramori. We're discussing a practical look at cardiorenal protection for CKD and type 2 diabetes.

Wow, thank you, Luiza. It is a bit more complex, but I think some – the kind of patients we really see day to day. So that was very, very helpful and sort of showing how careful you are in managing this case, especially with regards to potassium and so on, compared to your case, and the starting doses and everything. So thank you, Luiza.

Ana María, what do you think?

**Dr. Cebrián-Cuenca:**
Yes, I agree with you that it's a complex case. But we can do things for these kind of patients. If we put this patient in the KDIGO heat map, we have a patient at very high risk of cardiovascular and renal events and very high rates of mortality. And now we can do things for this kind of patient. We can reduce these risks. So it's very important just we keep these patients in mind because we can do things for these patients.

The KDIGO guidelines and the other guidelines recommend 3 classes of drugs to reduce the risk in these patients with chronic kidney disease and type 2 diabetes that are RAS [renin-angiotensin system] inhibitors, SGLT2 inhibitors, and also finerenone. Also the European Society of Cardiology guidelines recommend to reduce the cardiovascular and kidney failure risk, 3 things: SGLT2 inhibitors, blood pressure control, and also finerenone.

So here we have a typical case that we can do things for this patient and reduce the risk they have because of their kidney.

**Dr. Caramori:**
Yeah, I do agree, if I can chime in just for a second here. So what we usually use, Carolyn, is we consider normal values that go up to 30 mg of albumin per gram of creatinine if we use a spot urine collection, and the values that are stacked on albuminuria start at 30. Again, that's divided between low albuminuria, or the old term perhaps that we used was microalbuminuria, and that goes up to 300. And then at 300 mg/g, we start what would be called macroalbuminuria, or high albuminuria, or that's the equivalent of proteinuria for our patients. That would be the 300 mg/g is the equivalent of 500 mg of protein in the urine in general. So that's why we sometimes refer to it as proteinuria as well.

So all these patients that have albuminuria, so starting at 30, they have higher risk, the ones at 300 have an even greater risk. And as your eGFR declines – and we start from stage 1 to stage 5, where stage 5 is end-stage renal disease, with a need for transplant or dialysis, and patients really have eGFR lower than 15, that's stage 5. So that's where these patients move towards higher albuminuria and lower eGFR, as you move that direction, both your renal risk for progression towards end-stage renal disease and also cardiovascular risk significantly increased.

**Dr. Lam:**
Thank you so much. So 30/300, I think we can remember that. So thank you.

Pam, one other question, though. In your patient, you know, the poor patient couldn't tolerate the SGLT2 inhibitor. But in a case like this, and we've gone through the guidelines that say perhaps we should consider both the SGLT2 inhibitor and finerenone, are you comfortable starting both at the same time, and why not?

**Dr. Taub:**
So in my clinical practice – because when I see the patient, it's when they're very engaged and because follow-up sometimes takes a long time, patients sometimes don't have easy access – what I do is I try to start all the medications, but I have them stagger it. So I'll give them instructions and say, "Start the SGLT2 inhibitor. If no side effects after 2 weeks, start the finerenone." I typically don't start both together, because if they do have a side effect, sometimes it's hard to figure out exactly where the side effect is coming from. But it's really nice to use SGLT2 inhibitors and finerenone together, there's some data that says that there's some synergy there, and there's actually decreased incidence of hyperkalemia. So I love using that combination.

**Dr. Caramori:**
Yeah, I would say that I agree with Pam, and now we don't yet have data saying that we can start these agents together, but we will. So there is an ongoing trial that will answer that question if it's safe to start both agents at the same time. And I'm guessing here that the answer will be yes because, as Pam mentioned, we may have a beneficial effect to reduce the risk of hyperkalemia. That's of course more important in those who have a reduced eGFR to start with. So you may get some extra beneficial effect on the risk of hyperkalemia there.

And we may have a synergistic effect on reducing urinary albumin. So that's going to answer an important question. I do the same in practice. I start with medication, tell the patient that if everything's going well we will start the next in sequence, just to keep things moving. And we do the same with medications when we are managing hyperglycemia per se, for example, right? We know that patients

have elevated levels, and we will need to add some other medications without them or to ramp up on doses or to add another medication in the interim, and we check them quickly if needed for labs, sometimes without having an appointment, just to facilitate care for these patients so that they don't wait months and months until the new medication or a higher dose is introduced.

**Dr. Cebrián-Cuenca:**
I am in agreement with your comments. And also you have to make an effort just to avoid inertia. Because sometimes if you are doing the things step by step, some colleagues can do inertia. And it's very important just to treat these kind of patients.

**Dr. Lam:**
So, Ana María, I want to pick up on that point again about the inertia that you brought up. I think it's very important. But I also have to say I think physicians, other than inertia, also have a fear of causing risk that they don't quite understand. So, you know, especially when it's a new medication, and so on. So could you elaborate a little bit on what you, in practice, first look for in terms of safety and perhaps warn the patient as you start finerenone?

**Dr. Cebrián-Cuenca:**
I think it's very important to talk with our patients about what they should expect of the drug that we are prescribing, the positive effects and also talk about the adverse effects that they can experience. And it's very important, yes, to tell them that we have to monitor potassium and eGFR. It's very important to talk to them, that in 1 month time, we are going to ask for a blood test with potassium and also eGFR, and give them the pathology that we are going to follow.

**Dr. Lam:**
Wow. Thank you. And could you give us perhaps some specifics about what the guidelines say, maybe some, you know, alarm bells should ring when potassium levels are a certain level or how often to monitor?

**Dr. Cebrián-Cuenca:**
Yes, we have to do it simple. And I think it's very important just to keep in mind that we have to start finerenone when we have a potassium level less than 5. We have to stop finerenone with a potassium level more than 5.5. And we can initiate with a eGFR more than 25. One month after we start the finerenone, if the eGFR decline is less than 30, we can increase it also. If we have to start with 10, we can increase to 20. And if the potassium level is less than 4.8, we continue with the dose or increase if necessary. If the potassium level is between 4.8 and 5.5, we maintain the dose. And if we have, as I have said before, if we have potassium levels more than 5.5, we stop the treatment. And after, we have to do the blood test again and reintroduce when the potassium level is less than 5.

**Dr. Lam:**
Wow, that was very, very helpful. I think very reassuring to go through that. Thank you, Ana María.

Luiza perhaps could you also share, you know, even as we're thinking now of how to use this in practice, what to look out for, how to monitor, how do you identify the right patient that we should quickly start this on?

**Dr. Caramori:**
Yeah, I think that really starts with screening our patients. And we have been talking about this for a long time. And we saw in the case that Pam presented, again, that the patient had a completely normal eGFR, but had increased urine albumin level. So it's really important that we check both to get a creatinine so that we get an estimation of the patient's glomerular filtration rate. But to also check the urinary albumin levels, it's very simple. We just need to ask them to do a spot urine. But for some reason, sometimes even when we order, patients don't get it done. So I think it's very important to talk to the patients and explain why we need that test too. I think that when that discussion takes place, why we are doing things, I think that's more likely that people will go to the lab and get that urine test done. It's very interesting. Sometimes they go to the lab and get the bloodwork done, but they don't collect the urine. So it's really important to have that conversation. So I think that's the basis to identify these patients. Of course, we know about family history, we know about obesity, we know about dyslipidemia, we know about everything else, but we need to have these measurements that will help us to stratify the risk and to guide us in terms of therapy.

So I think that we are in a time where we do have a lot to offer our patients, and that's really important. We were not at this stage 10 years back, right? So now we have a lot to offer. And it's important that we offer them the therapies that we can that we have accessible so that we can reduce their risk. And that is, as we mentioned earlier, Carolyn, it's not going to be done by using a single agent. It's really a multidisciplinary approach. And we need to have colleagues involved, and need to have the patient very involved on that approach and understand that we may need to use multiple medications to really significantly reduce the risk of cardiovascular and renal disease in a meaningful way.

**Dr. Lam:**
That's so beautifully put, isn't it? So, Luiza, if I may, you talked about identifying the right patients, making sure we give the right

treatment. But I really love what both of you emphasized about communicating. So making sure we communicate to the patient the benefit/risk, and the benefit is huge. It's cardiorenal protection from real events. And then the risk. But the nice thing, it's a manageable risk, that if we monitor properly, we can manage it together with the patient, but please, they need to help us and not just skip all the tests and so on and so forth. Right?

Pam, anything else, pearls of wisdom to add?

**Dr. Taub:**
I think it's all about starting early and detecting disease early. That's where the elegance of medicine is, is detecting disease before it's obvious. So detecting that microalbuminuria before the eGFR starts to decline and acting on that.

**Dr. Lam:**
All right, well, this has really been an incredibly helpful and educational discussion. Thank you so much, Pam, Ana María, Luiza. Could I now give each of you just a chance to give your take-home messages to everyone? I could start with Luiza first, please?

**Dr. Caramori:**
Sure, I need to echo what Pam said, important to check urinary albumin, but please don't forget to get a creatinine and get an estimated GFR. Because the same way that we have patients who have albuminuria and have a normal GFR, we do have patients who have no albuminuria but have a reduced eGFR. So both these factors exist, so it's important to check both.

**Dr. Lam:**
Thank you. Ana María?

**Dr. Cebrián-Cuenca:**
Yes, I agree. And my message is early intervention, please. Check the kidney of all of your patients with both eGFR and also albuminuria; think in both. Keep in mind the risk your patients have because of the kidney and act when you need for treat this risk and reduce the risk of your patients.

**Dr. Lam:**
Thank you. And, Pam?

**Dr. Taub:**
Well, in addition to early detection, aggressive treatment with the multiple agents that we have available is paramount. And don't be afraid of the side effects like hyperkalemia—just have a strategy for close monitoring.

**Dr. Lam:**
Thank you. I don't think I could add anything more except to thank you, Pam, Ana María, Luiza, once again. And to thank the audience for listening in today. It has been a very valuable time and I have learned a lot. I trust the audience has, too. Thank you.

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